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Toxicological Profile for Dibenz(a,h)Anthracene

ICF-Clement, Washington, DC

Prepared for:

Agency for Toxic Substances and Disease Registry
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Toxicological Profile for

DIBENZ[a,h]ANTHRACENE

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

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The ATSDR Toxicological Profile for Dibenzo(a,h)anthracene is intended to characterize succinctly the toxicological and health effects information for the substance. It identifies and reviews the key literature that describes the substances's toxicological properties. Other literature is presented but described in less detail. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced. The profile begins with a public health statement, which describes in nontechnical language the substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine the substance's health effects is described. Research gaps in nontoxic and health effects information are described. Research gaps that are of significance to the protection of public health will be identified in a separate effort. The focus of the document is on health and toxicological information.

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FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The list of the 100 most significant hazardous substances was published in the *Federal Register* on April 17, 1987.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

> "(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

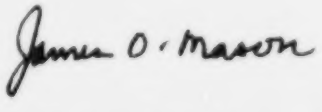
This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Research gaps in toxicologic and health effects information are described in the profile. Research gaps that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents in response to public comments and as additional data become available; therefore, we encourage comment that will make the toxicological profile series of the greatest use.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



James O. Mason, M.D., Dr. P.H.
Assistant Surgeon General
Administrator, ATSDR

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1. PUBLIC HEALTH STATEMENT

1.1 WHAT IS DIBENZ[a,h]ANTHRACENE?

Dibenz[a,h]anthracene (DB[a,h]A) is one of the polycyclic aromatic hydrocarbon (PAH) compounds. Because it is formed when gasoline, garbage, or any animal or plant material burns, it is usually found in smoke and soot. This chemical combines with dust particles in the air, and is carried into water and soil and onto crops. Dibenz[a,h]anthracene is found in the coal tar pitch that industry uses to join electrical parts together. It is also found in creosote, a chemical used to preserve wood.

1.2 HOW MIGHT I BE EXPOSED TO DIBENZ[a,h]ANTHRACENE?

People may be exposed to DB[a,h]A from environmental sources such as air, water, and soil and from cigarette smoke and cooked food. Workers who handle or are involved in the manufacture of PAH-containing materials may also be exposed to DB[a,h]A. Typically, exposure for workers and the general population is not to DB[a,h]A alone but to a mixture of similar chemicals.

The general population may be exposed to dust, soil, and other particles that contain DB[a,h]A. The largest sources of DB[a,h]A in the air are open burning and home heating with wood and coal. Factories that produce coal tar also contribute small amounts of DB[a,h]A to the air. People may come in contact with DB[a,h]A from soil on or near hazardous waste sites, such as former gas-manufacturing sites or abandoned wood-treatment plants that used creosote. At this time, DB[a,h]A has been found at 16 out of 1,177 sites on the National Priorities List (NPL) of hazardous waste sites in the United States. As more sites are evaluated by the Environmental Protection Agency (EPA), this number could change. The soil near areas where coal, wood, or other products have been burned is another source of exposure. Exposure to DB[a,h]A and other PAHs may also occur through skin contact with products that contain PAHs such as creosote-treated wood, asphalt roads, or coal tar.

People may be exposed to DB[a,h]A by drinking water from the drinking water supplies in the United States that have been found to contain low levels of the chemical. Foods grown in contaminated soil or air may contain DB[a,h]A. Cooking food at high temperatures, as occurs during charcoal-grilling or charring, can increase the amount of DB[a,h]A in the food. Dibenz[a,h]anthracene has been found in cereals, vegetables, fruits, meats, beverages, and in cigarette smoke.

The greatest exposure to DB[a,h]A is likely to take place in the workplace. People who work in coal tar production plants; coking plants; asphalt production plants; coal-gasification sites; smoke houses; municipal trash incinerators; and facilities that burn wood, coal, or

oil may be exposed to DB[a,h]A in the workplace air. Dibenz[a,h]anthracene may also be found in areas where high temperature food fryers and broilers are used.

1.3 HOW DOES DIBENZ[a,h]ANTHRACENE GET INTO MY BODY?

The most common way DB[a,h]A enters the body is through the lungs when a person breathes in air or smoke containing it. It also enters the body through the digestive system when substances containing it are swallowed. Although DB[a,h]A does not normally enter the body through the skin, small amounts could enter if contact occurs with soil that contains high levels of DB[a,h]A (for example, near a hazardous waste site) or if contact is made with heavy oils containing DB[a,h]A.

1.4 HOW CAN DIBENZ[a,h]ANTHRACENE AFFECT MY HEALTH?

Dibenz[a,h]anthracene causes cancer in laboratory animals when applied to their skin. This finding suggests that it is likely that people exposed in the same manner could also develop cancer.

Because studies of DB[a,h]A are not complete, we don't know whether DB[a,h]A that is breathed in or swallowed could cause cancer or whether it can cause harmful effects other than cancer.

1.5 IS THERE A MEDICAL TEST TO DETERMINE IF I HAVE BEEN EXPOSED TO DIBENZ[a,h]ANTHRACENE?

Very few tests are available that can tell if exposure to DB[a,h]A has taken place. In the body, DB[a,h]A is changed to related chemical substances called metabolites. The metabolites can bind with DNA, the genetic material of the body. The body's response after exposure can be measured in the blood. However, this test is still being developed. Dibenz[a,h]anthracene can also be found in the urine of individuals exposed to PAHs. It is not possible to know from these tests how much DB[a,h]A a person was exposed to or to predict what health effects may happen at certain levels. Also, none of these tests have been used in exposure situations outside the workplace.

1.6 WHAT LEVELS OF DIBENZ[a,h]ANTHRACENE EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

No information has been found about specific levels of DB[a,h]A that have caused harmful effects in people after breathing, swallowing, or touching the substance.

Skin cancer has developed in mice that had DB[a,h]A on their skin throughout their lives. Skin cancer is the only harmful effect that can be predicted when animals are exposed to DB[a,h]A. It is not known whether similar levels could cause cancer in people. No information has been found about harmful effects of DB[a,h]A in animals that breathed in or ate the chemical.

1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

Based on information from another PAH chemical, the federal government has developed standards and guidelines to protect individuals from the potential health effects of PAHs, including DB[a,h]A, in drinking water. EPA has provided estimates of levels of total cancer-causing PAHs in lakes and streams associated with various risks of developing cancer in people. EPA has also determined that any release of PAHs of more than 1 pound should be reported to the National Response Center.

Pure DB[a,h]A is produced in the United States only as a laboratory chemical. However, DB[a,h]A is a PAH, and PAHs are found in coal tar and in the creosote oils and pitches formed from the production of coal tar. The government's goal has been to protect workers involved with the production of coal tar products. Although government standards are not for DB[a,h]A alone, they are useful in controlling exposure to total PAHs.

The National Institute for Occupational Safety and Health (NIOSH) has determined that workplace exposure to coal products can increase the risk of lung and skin cancer in workers and suggests a workplace exposure limit for coal tar products of 0.1 milligram of PAHs per cubic meter of air (0.1 mg/m^3) for a 10-hour workday, 40-hour workweek. NIOSH has not suggested a specific workplace limit for DB[a,h]A. The Occupational Safety and Health Administration (OSHA) has set a legal limit of 0.2 milligram of all PAHs per cubic meter of air (0.2 mg/m^3).

2. HEALTH EFFECTS SUMMARY

2.1 INTRODUCTION

This section summarizes and graphs data on the health effects concerning exposure to DB[a,h]A. The purpose of this section is to present levels of significant exposure for DB[a,h]A based on key toxicological studies, epidemiological investigations, and environmental exposure data. The information presented in this section is critically evaluated and discussed in Sect. 4, Toxicological Data, and Sect. 7, Potential for Human Exposure.

This Health Effects Summary section comprises two major parts. Levels of Significant Exposure (Sect. 2.2) presents brief narratives and graphics for key studies in a manner that provides public health officials, physicians, and other interested individuals and groups with (1) an overall perspective of the toxicology of DB[a,h]A; and (2) a summarized depiction of significant exposure levels associated with various adverse health effects. This section also includes information on the levels of DB[a,h]A that have been monitored in human fluids and tissues and information about levels of DB[a,h]A found in environmental media and their association with human exposures.

The significance of the exposure levels shown on the graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of overt clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with frank effects (Frank Effect Level, FEL). Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (Lowest-Observed-Adverse-Effect Level, LOAEL) or exposure levels below which no adverse effects (No-Observed-Adverse-Effect Level, NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels) are of interest to health professionals and citizens alike.

Adequacy of Database (Sect. 2.3) highlights the availability of key studies on exposure to DB[a,h]A in the scientific literature and displays these data in three-dimensional graphs consistent with the format in Sect. 2.2. The purpose of this section is to suggest where there might be insufficient information to establish levels of significant human exposure. These areas will be considered by the Agency for Toxic Substances and Disease Registry (ATSDR), EPA, and the National Toxicology Program (NTP) of the U.S. Public Health Service in order to develop a research agenda for dibenz[a,h]anthracene.

2.2 LEVELS OF SIGNIFICANT EXPOSURE

2.2.1 Key Studies and Graphical Presentations

To help public health professionals address the needs of persons living or working near hazardous waste sites, the toxicology data summarized in this section are organized first by route of exposure--inhalation, ingestion, and dermal--and then by toxicological end points that are categorized into six general areas--lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, genetic toxicity, and carcinogenicity. The data are discussed in terms of three exposure periods--acute, intermediate, and chronic.

Two kinds of graphs are used to depict the data. The first type is a "thermometer" graph. It provides a graphical summary of the human and animal toxicological end points and levels of exposure for each exposure route for which data are available. The ordering of effects does not reflect the exposure duration or species of animal tested. The second kind of graph shows Levels of Significant Exposure (LSE) for each route and exposure duration. The points on the graph showing NOAELs and LOAELs reflect the actual doses (levels of exposure) used in the key studies. No adjustments for exposure duration or intermittent exposure protocol were made.

Adjustments reflecting the uncertainty of extrapolating animal data to man, intraspecies variations, and differences between experimental versus actual human exposure conditions were considered when estimates of levels posing minimal risk to human health were made for noncancer end points. These minimal risk levels were derived for the most sensitive noncancer end point for each exposure duration by applying uncertainty factors. These levels are shown on the graphs as a broken line starting from the actual dose (level of exposure) and ending with a concave-curved line at its terminus. Although methods have been established to derive these minimal risk levels (Barnes et al. 1987), shortcomings exist in the techniques that reduce the confidence in the projected estimates. Also shown on the graphs under the cancer end point are low-level risks (10^{-4} to 10^{-7}) reported by EPA if available. In addition, the actual dose (level of exposure) associated with the tumor incidence is plotted.

2.2.1.1 Inhalation exposure

No information was located in the available literature concerning the effects of DB[a,h]A following inhalation exposure.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. Only one study was available using *Drosophila melanogaster*. DB[a,h]A exposure via inhalation resulted in positive activity in the sex-linked recessive lethal test (Demerec 1948).

Carcinogenicity. No reports directly correlating inhalation exposure to DB[a,h]A and cancer induction are available, although reports of cancer among individuals exposed to mixtures of polycyclic aromatic hydrocarbons containing DB[a,h]A lend qualitative support to its potential for carcinogenicity in humans. No inhalation experiments in animals are available, although DB[a,h]A has elicited respiratory tract tumors in rats and hamsters following intratracheal instillation.

2.2.1.2 Oral exposure

Adequate information was not available in existing literature to determine the effects of DB[a,h]A following oral exposure. Several studies exist in animals; however, they were judged to be inadequate to support the development of significant human exposure levels, although they provide some suggestion of DB[a,h]A's carcinogenicity by the oral route.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No information is available on the carcinogenicity of DB[a,h]A to humans following oral exposure.

Several studies of the oral carcinogenicity of DB[a,h]A in animals were located; however, these studies were flawed and judged to be inadequate to support the development of significant human exposure levels.

2.2.1.3 Dermal exposure

No information is available on the effects of short-term dermal exposures of DB[a,h]A on humans. There are reports in the literature that DB[a,h]A suppresses the sebaceous glands in mouse skin following topical application (Bock and Mund 1958). However, these studies failed to employ control groups, and, therefore, definitive conclusions concerning the dermal toxicity of DB[a,h]A cannot be made.

DB[a,h]A has been shown to be carcinogenic following long-term dermal exposure. This conclusion is based on observations of laboratory animals since no data are available for human exposure. The results are summarized in Figs. 2.1 and 2.2.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No information directly correlating human dermal exposure to DB[a,h]A and cancer induction is available, although reports

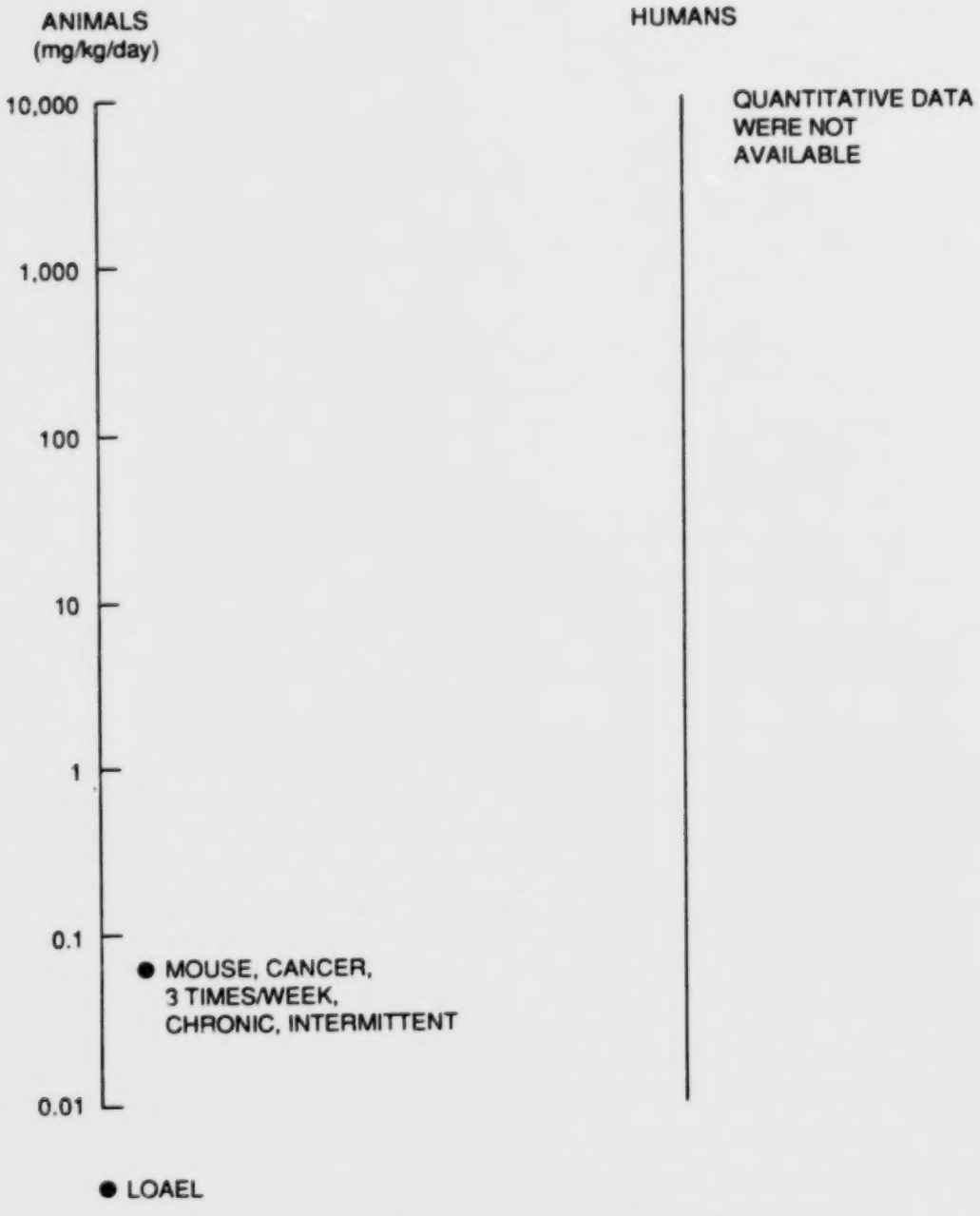


Fig. 2.1. Effects of dibenz[a,h]anthracene—dermal exposure.

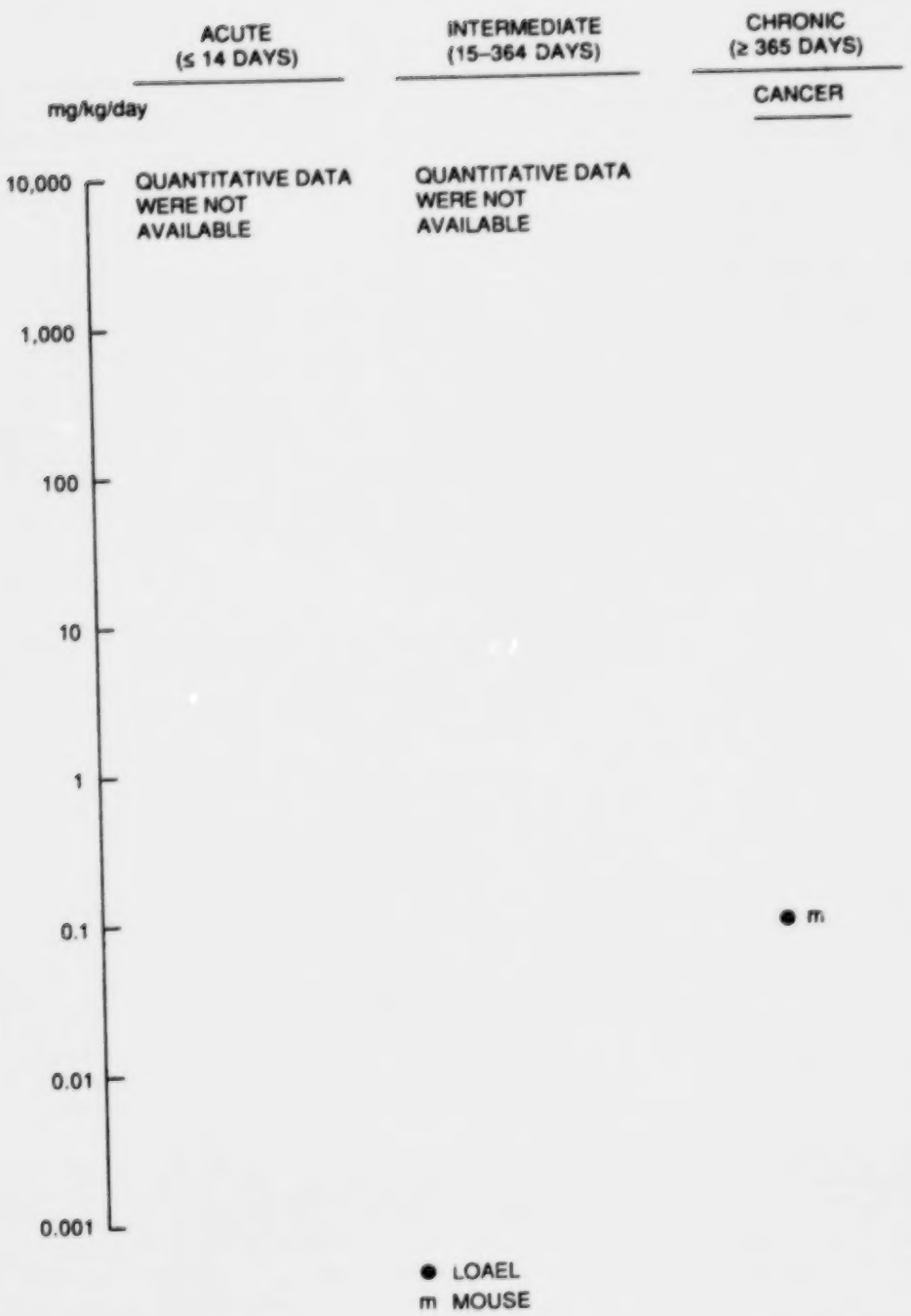


Fig. 2.2. Levels of significant exposure for dibenz[a,h]anthracene—dermal.

of skin tumors among individuals exposed to mixtures of polycyclic aromatic hydrocarbons containing DB[a,h]A lend qualitative support to its potential for carcinogenicity in humans.

Studies in experimental animals have demonstrated the ability of DB[a,h]A to induce skin tumors following long-term dermal exposure. Mice receiving doses of 0.029 mg/kg and larger applied to their skin three times weekly developed an excess of skin tumors following long-term exposure (Wynder and Hoffmann 1959, Van Duuren et al. 1967). No estimate of human risk has been calculated.

2.2.2 Biological Monitoring

The available biological monitoring techniques can be useful in predicting whether exposure to DB[a,h]A or other PAHs has occurred, but they may not be useful in estimating body doses because there have been no population-based studies to determine normal body levels of PAHs. Individual variability, confounding effects of drugs, and specificity of the techniques are likely to complicate the association between DB[a,h]A metabolites in the body and environmental exposure. The most common test for determining exposure to PAHs include examination of tissues, blood, and urine for the presence of PAHs or PAH metabolites. Currently available biological monitoring techniques are discussed in detail in Sect. 8.

Modica et al. (1982) and Bartosek et al. (1984) used gas-liquid chromatography to determine the presence of PAHs in the blood, mammary and adipose tissue, liver, and brain of rats. However, examples of examination of human tissue samples using this method were not located in the available literature.

In the body, DB[a,h]A can be converted by specific cellular enzymes to a dihydrodiol and further metabolized to diol epoxides and K-region oxides that can bind to DNA and form DNA adducts (MacNicoll et al. 1979). In the ^{32}P postlabeling technique, a tissue sample is taken from an exposed individual, and DNA from the exposed cells is digested and labeled with radioactive phosphorus (^{32}P). Thin-layer chromatography is then used to determine the presence of altered DNA, and scintillation counting is used to quantify the adducts (Randerath et al. 1985). The diol epoxide adducts can also be removed from DNA and quantified using high-performance liquid chromatography (Phillips et al. 1979, Liptay-Reuter et al. 1985). Although the presence of DNA adducts is directly associated with exposure to DB[a,h]A, this technique of analyzing adducts is limited in its usefulness to predict body dose from environmental exposure because individual biochemistry may affect the conversion of DB[a,h]A to diol epoxides. A technique has been developed that tests for the presence of antibodies to the PAH diol epoxide-DNA adducts in blood using immunoassays (Harris 1985a,b; Harris et al. 1985, 1986). A patent application has been submitted for a method and kit for detecting antibodies in human sera to PAH diol epoxide-DNA adducts by immunoassay (Harris 1985b). This method has been used to examine exposure to benzo[a]pyrene and other polycyclic hydrocarbons.

PAHs or PAH metabolites have been detected in the urine of individuals occupationally exposed to atmospheric PAHs and in

individuals treated with therapeutical coal tar for psoriasis (Becher and Bjorseth 1983, Becher et al. 1984, Clonfero et al. 1986).

A recent technique using an antibody-based fiberoptics biosensor has been tested to detect PAHs. This technique has been investigated in sample solutions containing benzo[a]pyrene and may be useful for assessing an individual's exposure to other PAHs provided appropriate antibodies are used (Vo-Dinh et al. 1987).

2.2.3 Environmental Levels as Indicators of Exposure and Effects

2.2.3.1 Levels found in the environment

As with other PAHs, DB[a,h]A can occur in air, water, soil, and food. However, adequate data are not available to characterize background DB[a,h]A concentrations in the nonoccupational environment. No studies are available in which DB[a,h]A was monitored in the air of U.S. cities, and only one study (Sorrell et al. 1981) is available in which DB[a,h]A was detected in finished drinking waters of the United States at concentrations of less than 2 ng/L. No data are available on background DB[a,h]A levels in soil, but concentrations of total polycylic aromatic hydrocarbons have been reported in the range of 4 to 13 mg/kg in relatively rural areas of the United States (summarized by Blumer et al. 1977).

DB[a,h]A is expected to contaminate the soil and be deposited on particulate air matter in the area surrounding abandoned waste sites, such as former manufactured gas plants and creosote wood treating facilities.

Data are not available which relate environmental levels to significant health effects in humans following exposures.

2.2.3.2 Human exposure potential

Although little or inadequate monitoring data are available, it is expected that humans may be exposed to DB[a,h]A in the air, water, soil, and food. Each of these media is believed to constitute a normal route of background exposure. Background exposures to DB[a,h]A are expected to be at very low levels. Much higher exposure concentrations are associated with tobacco smoke and with some occupational environments. At hazardous waste sites, exposure concentrations also may be higher, and humans will most likely be exposed to DB[a,h]A via contact with soil or inhalation of particulate matter in air. Estimates of body doses or tissue levels associated with DB[a,h]A intake require: (1) information on the chemical concentrations in soil and air, (2) certain assumptions about factors controlling intake, and (3) information on absorption of DB[a,h]A from soil or particulate matter.

Information on the first two of these data needs is relatively site-specific in nature and cannot be generalized across all sites. Quantitative toxicological information on absorption of DB[a,h]A and other PAHs from soil or particulate matter is lacking, although absorption is expected to be low (Becher et al. 1984). Consequently, estimates of dose following exposure to DB[a,h]A in soil or air are based on assumptions regarding dermal absorption from soil and

absorption of incidentally ingested DB[a,h]A on soil or particulate matter or inhaled DB[a,h]A on particulate matter. These assumptions lend uncertainty to any risk assessment of potential health effects following environmental exposures.

2.3 ADEQUACY OF DATABASE

2.3.1 Introduction

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each of the 100 most significant hazardous substances found at facilities on the CERCLA National Priorities List. Each profile must include the following content:

"(A) An examination, summary and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This section identifies gaps in current knowledge relevant to developing levels of significant exposure for DB[a,h]A. Such gaps are identified for certain health effect end points (lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, and carcinogenicity) reviewed in Sect. 2.2 of this profile in developing levels of significant exposure for DB[a,h]A, and for other areas such as human biological monitoring and mechanisms of toxicity. The present section briefly summarizes the availability of existing human and animal data, identifies data gaps, and summarizes research in progress that may fill such gaps.

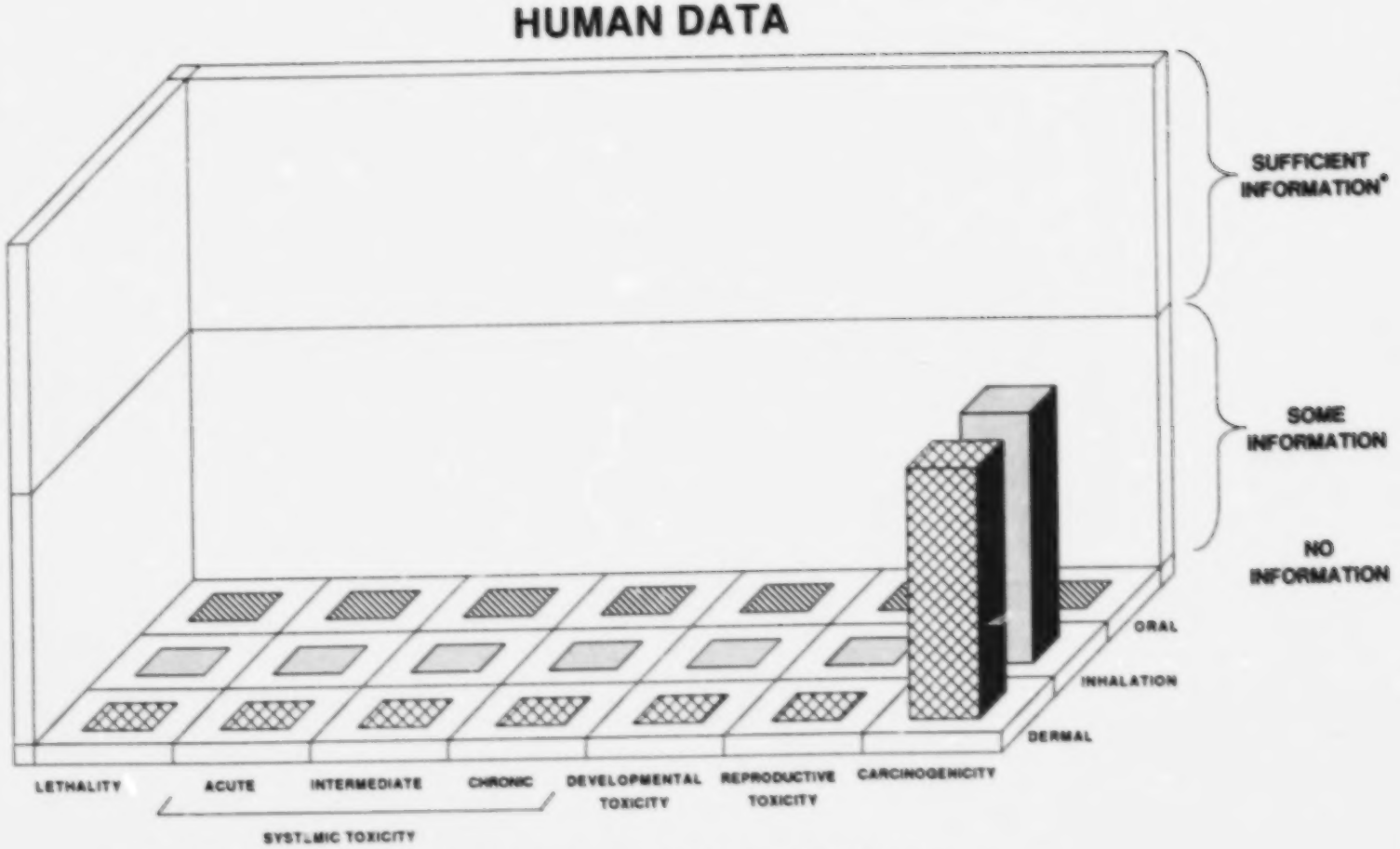
Specific research programs for obtaining data needed to develop levels of significant exposure for DB[a,h]A will be developed by ATSDR, NTP, and EPA in the future.

2.3.2 Health Effect End Points

2.3.2.1 Introduction and graphic summary

The availability of data for health effects in humans and animals is depicted on bar graphs in Figs. 2.3 and 2.4, respectively.

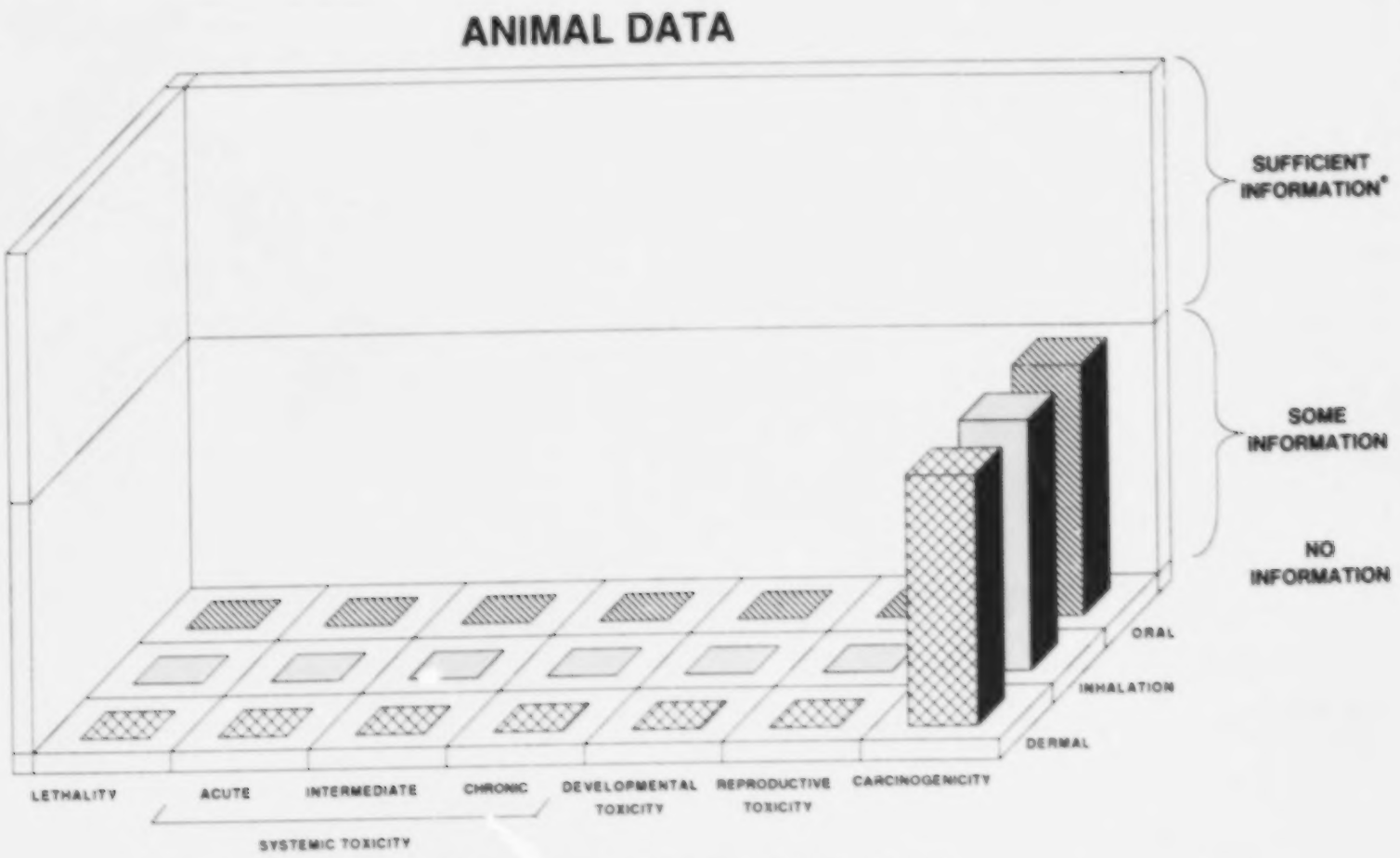
The bars of full height indicate that there are data to meet at least one of the following criteria:



*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Note: The adequacy of the database for the carcinogenicity of dibenz[a,h]anthracene by the inhalation and dermal routes of exposure has been assessed on the basis of human exposure to complex mixtures of chemicals containing this compound, not on the basis of the compound alone.

Fig. 2.3. Availability of information on health effects of dibenz[a,h]anthracene (human data).



*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Note: The adequacy of the database for the carcinogenicity of dibenz[a,h]anthracene by the inhalation route of exposure has been assessed on the basis of intratracheal instillation experiments using hamsters and rats, in the absence of inhalation data.

Fig. 2.4. Availability of information on health effects of dibenz[a,h]anthracene (animal data).

1. For noncancer health end points, one or more studies are available that meet current scientific standards and are sufficient to define a range of toxicity from no effect levels (NOAELs) to levels that cause effects (LOAELs or FELs).

2. For human carcinogenicity, a substance is classified as either a "known human carcinogen" or "probable human carcinogen" by both EPA and International Agency for Research on Cancer (IARC) (qualitative), and the data are sufficient to derive a cancer potency factor (quantitative).

3. For animal carcinogenicity, a substance causes a statistically significant number of tumors in at least one species and the data are sufficient to derive a cancer potency factor.

4. There are studies which show that the chemical does not cause this health effect via this exposure route.

Bars of half height indicate that "some" information for the end point exists, but does not meet any of these criteria.

The absence of a column indicates that no information exists for that end point and route.

2.3.2.2 Description of highlights of graphs

Figure 2.3 indicates that there are no data available to assess significant exposure levels of DB[a,h]A for humans. Reports of adverse health effects, such as carcinogenicity by the inhalation and dermal routes of exposure, do exist for mixtures of chemicals that include DB[a,h]A, providing some information to qualitatively assess the role of DB[a,h]A as a human carcinogen.

As displayed in Fig. 2.4, some data are available in animals to assess only the dermal, oral, and inhalation carcinogenicity of DB[a,h]A; the latter is based on intratracheal instillation experiments, however, in the absence of inhalation data. The studies of the oral carcinogenicity of DB[a,h]A were considered inadequate to support the development of significant human exposure levels. No information could be located on the effects of DB[a,h]A following inhalation exposure.

2.3.2.3 Summary of relevant ongoing research

Studies of the biological mechanisms of action of PAHs and their molecular chemistry are being conducted in a number of laboratories. In particular, Dr. D. M. Jerina of the National Institutes of Health is conducting research on the enzymatic oxidation of DB[a,h]A to its carcinogenic metabolites and is synthesizing its known and potential proximate and ultimate carcinogenic derivatives. A comparative potency method to quantitatively assess the carcinogenic effects for PAHs is under development by the Carcinogen Assessment Group, the Office of Solid Waste, the Office of Drinking Water, and the Office of Air Quality Planning and Standards of the EPA (EPA Contract Number 68-02-4403) and is being applied to the data available for DB[a,h]A.

2.3.3 Other Information Needed for Human Health Assessment

2.3.3.1 Toxicokinetics and mechanisms of action

The metabolism of DB[a,h]A has been examined in microsomal preparations and organ cultures. The level and detail of information available on DB[a,h]A are considerably limited relative to information on benzo[a]pyrene. There is no adequate database from which to estimate absorption parameters for any of the relevant exposure routes. It is questionable as to whether the toxicokinetic database developed for benzo[a]pyrene could be used for DB[a,h]A. It has been postulated that there are significant differences in the rates at which these two hydrocarbons are metabolized and that metabolism plays an important role in the absorption of aromatic hydrocarbons (Heidelberger and Weiss 1951, Sanders et al. 1986, Kao et al. 1985), particularly from the lungs and skin (Creasia et al. 1976, Tornquist et al. 1985, Medinsky and Kampcik 1985). No current studies were identified that would provide the desired toxicokinetic data.

DB[a,h]A undergoes metabolic transformations in animals to reactive intermediates responsible for its toxicity. No information on biotransformation of DB[a,h]A in humans is available. In animals, DB[a,h]A is metabolized to a bay-region 3,4-dihydrodiol-1,2-epoxide derivative which is thought to be responsible for its genotoxic and carcinogenic activity.

2.3.3.2 Adequacy of data on biological monitoring

The biological monitoring techniques in which DNA adducts are quantified are limited in determining environmental exposure because inborn factors, environmental chemistry, and drugs can alter the activity of the enzymes responsible for converting DB[a,h]A to the diol epoxides that bind to DNA. There is a lack of information concerning the use of these techniques in occupationally or environmentally exposed individuals. Additional research should include further investigation of the formation and determination of adducts following exposure.

The technique that uses immunoassays to determine the presence of antibodies to PAH-DNA adducts in blood has been examined in occupationally exposed individuals and smokers (Harris 1985b). This technique has reported an association between sera positive for antibodies and occupational exposure or smoking. The reliability of this method needs to be examined further in other, nonoccupational, exposure situations.

The presence of PAHs or PAH metabolites in urine is an indication that exposure has occurred. However, in occupational studies, the amount of PAH concentrated in the urine did not adequately reflect environmental PAH concentrations (Becher and Bjorseth 1983, Becher et al. 1984). This discrepancy was reported to result from the nonbioavailability of particle-bound PAH, and therefore this method should be further examined for its applicability in other exposure situations.

In addition, smoking cigarettes and some occupationally related activities result in human exposure to PAHs; therefore, the

determination of biological levels of PAHs in smokers and in the general population must be further examined to properly assess environmental or occupational exposure.

2.3.3.3 Environmental considerations

The accuracy and precision of the analytical methods used to measure ambient DB[a,h]A are somewhat limited. But the current methods, if properly conducted, are sufficient to record ambient levels of DB[a,h]A. However, some methods have limited sensitivity.

No data are available to adequately characterize background levels of DB[a,h]A or levels typically found at hazardous waste sites. Comprehensive monitoring studies are being conducted by EPA at or around many hazardous waste sites, but the data are not yet available in a single database.

No data are available on the bioavailability of DB[a,h]A in soil or adsorbed onto particulate matter in air. This lack of information limits our understanding of potential health risks to humans following exposure to these media.

Information on the fate of DB[a,h]A adsorbed onto particulate matter in air is presently unclear. The role of photochemical oxidation in the removal of DB[a,h]A from air needs to be elucidated. Also, additional information on biodegradation processes and rates in aquatic and terrestrial systems is needed.

Only limited information is available on the interactions of DB[a,h]A in vivo and with other chemicals typically found in the environment and at hazardous waste sites. Consequently, risks associated with exposure to DB[a,h]A in the environment are not completely understood.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The chemical formula, structure, synonyms, and identification numbers for DB[a,h]A are listed in Table 3.1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of DB[a,h]A are given in Table 3.2.

Table 3.1. Chemical identity of dibenz[a,h]anthracene

Chemical name: Dibenz[a,h]anthracene

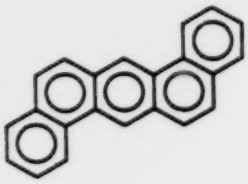
Synonyms: 1,2:5,6-dibenzanthracene;
1,2,5,6-dibenzanthracene; 1,2:5,6-dibenz[a]anthracene;
1,2:5,6-dibenzoanthracene;
dibenzo[a,h]anthracene; DB[a,h]A; DBA (IARC 1983)[a]

Trade name: Not applicable

Chemical formula: $C_{22}H_{14}$ (IARC 1983)

Wiswesser line notation: L G6 D6 B666J (HSDB 1987)

Chemical structure:



Identification numbers:

CAS Registry No.: 53-70-3
NIOSH RTECS No.: HN2625000
EPA Hazardous Waste No.: U063
OHM-TADS No.: Not available
DOT/UN/NA/IMCO Shipping No.: Not available
STCC No.: Not available
Hazardous Substances Data Base No.: 5097
National Cancer Institute No.: Not available

[a]Confusion exists in the literature concerning the naming of this compound, mainly due to the fact that two different systems (Richter and IUPAC) of numbering the anthracene ring structures have been used; the IARC reference, unfortunately, does not acknowledge that this confusion exists and that nomenclature for some of the synonyms listed is incorrect.

Table 3.2. Physical and chemical properties of dibenz[a,h]anthracene

Property	Value	References
Molecular weight	278.35 g/mol	CRC 1987
Color	Colorless	IARC 1983
Physical state	Plates (recrystallized from acetone) or leaflets (recrystallized from acetic acid)	CRC 1987
Odor	Not available	
Melting point	269-270°C	CRC 1987
Boiling point	Sublimes	
Autoignition temperature	Unknown	
Solubility		
Water	0.5 μg/L	IARC 1983
Organic solvents	Slightly soluble in ethyl alcohol; soluble in acetone, acetic acid, benzene, toluene, and xylene	CRC 1987
Biological fluids	Unknown	
Density	1.282	HSDB 1987
Partition coefficients octanol-water (K_{ow})	6.9×10^6	EPA 1982
Log K_{ow}	6.84	
Soil-organic carbon-water (K_{oc})	3.3×10^6	EPA 1982
Vapor pressure (20°C)	1×10^{-10} mm Hg	EPA 1982
Henry's law constant	7.3×10^{-8}	EPA 1982
Flashpoint	Unknown	
Flammability limits	Unknown	
Conversion factors	1 ppm (in air) = 11.39 mg/m^3[a]	Verschueren 1983

[a]Calculated using the ideal gas law, PV = nRT at 25°C.

4. TOXICOLOGICAL DATA

4.1 OVERVIEW

There is no toxicokinetic information available on dibenz[a,h]anthracene in humans. Experiments in animals indicate that DB[a,h]A is absorbed by the oral route of exposure; dermal absorption is slow, and inhalation absorption has not been studied. Absorbed DB[a,h]A is distributed to several tissues and is metabolized to conjugated derivatives to permit elimination, although it is excreted predominantly in the feces.

DB[a,h]A is metabolized to reactive bay-region diol-epoxide derivatives and K-region oxides that are thought to be responsible for its genotoxic and carcinogenic activity in experimental systems. DB[a,h]A is a carcinogen by the dermal route of exposure in laboratory animals. There is inconclusive evidence which suggests that DB[a,h]A is an experimental carcinogen by the oral route. Its carcinogenicity has not been studied by the inhalation route, although it has induced tumors following intratracheal instillation. Evidence from studies of complex mixtures of chemicals that include DB[a,h]A provides qualitative support of its carcinogenicity in humans by the inhalation and dermal routes. Mutation is thought to be a necessary (albeit insufficient) step for DB[a,h]A's carcinogenic activity.

There is no information on other toxic effects of DB[a,h]A in humans and experimental animals following inhalation, oral, and dermal exposures.

4.2 TOXICOKINETICS

4.2.1 Overview

There is no toxicokinetic information available on DB[a,h]A in humans. Experiments in animals indicate that DB[a,h]A is absorbed by the oral route; dermal absorption is relatively slow except in the presence of organic solvents; and no direct evidence is available for absorption of DB[a,h]A via the lungs. Absorbed DB[a,h]A is distributed to several tissues. The relative uptake is dependent on the blood perfusion rate of the tissue; initial concentrations are higher in the liver and kidney. DB[a,h]A shows a tendency to persist in the adrenals, ovaries, and adipose tissue.

DB[a,h]A undergoes metabolic transformations in animals to reactive intermediates responsible for its toxicity. No information on biotransformation of DB[a,h]A in humans is available. The principal metabolic intermediates formed include arene oxides, phenols, dihydrodiols, and a bay-region diol epoxide. DB[a,h]A-3,4-dihydrodiol is

metabolically activated to a biologically active intermediate whose structure has been proposed as a bay-region 3,4-dihydrodiol-1,2-epoxide.

DB[a,h]A is excreted predominantly in the feces. The excreted material contains a higher proportion of the hydrocarbon relative to similar compounds (benzo[a]pyrene, benz[a]anthracene). It is expected that the excreted metabolites of DB[a,h]A will be similar to those of other PAHs and will consist of phenols and dihydrodiols, either free or conjugated as glucuronide and sulfate esters, and glutathione conjugates.

The relatively low rate of oxidative metabolism of DB[a,h]A contributes to a slower rate of excretion when compared with other polycyclic aromatic hydrocarbons.

4.2.2 Absorption

4.2.2.1 Inhalation

Human. No quantitative information on the absorption of DB[a,h]A via the respiratory tract was found. Absorption of DB[a,h]A via this route is inferred from identification of DB[a,h]A and its metabolites in individuals exposed to polycyclic aromatic hydrocarbons in an industrial environment containing high levels of PAH in the atmosphere (Becher and Bjorseth 1983).

Animal. No information was found on the absorption of DB[a,h]A via the respiratory tract. By analogy to benzo[a]pyrene, pulmonary absorption of DB[a,h]A is expected to be efficient and to be subject to similar controlling factors. Specifically, the role of metabolism in absorption mechanisms, particle size, and mucociliary clearance is anticipated to influence the rate of absorption via the respiratory tract (Creasia et al. 1976, Tornquist et al. 1985, Medinsky and Kampcik 1985).

Sun et al. (1982) conducted a study on the biological fate and mechanisms of absorption of inhaled PAHs absorbed on particles in the rat using benzo[a]pyrene (B[a]P) as the representative PAH. A [^{3}H]-B[a]P concentration of 0.6 μg/L adsorbed on ultrafine Ga_2O_3 particles (diameter = 0.1 μm) was administered to rats as an aerosol. A parallel study was conducted with a pure [^{3}H]-B[a]P aerosol (no carrier) at a concentration of 1 μg/L. Total exposure time for both groups was 30 min. The amount of aerosol particles deposited in the lung after termination of exposure was approximately 20% for Ga_2O_3 (corresponding to 3% [^{3}H]-B[a]P) and approximately 10% for the pure hydrocarbon aerosol. These values represent the percentage of the total inhaled mass that was actually deposited in the lungs. The excretion of hydrocarbon was monitored for over 2 weeks, at which time a nearly quantitative recovery of radioactivity was obtained, indicating complete absorption of the initially deposited hydrocarbon. Consistent with administration of B[a]P by other routes, inhaled hydrocarbon was excreted predominantly in the feces (94% for B[a]P on Ga_2O_3 particles and 86% for the pure aerosol). Significant differences in the clearance times of Ga_2O_3-adsorbed and pure B[a]P strongly suggested that a substantial amount of B[a]P coated on Ga_2O_3 particles was cleared from the lungs by mucociliary clearance and subsequent ingestion. The pure B[a]P aerosol particles retained by

the lungs were cleared by absorption into the blood stream. In contrast, particle association of B[a]P increased the retention of B[a]P in the lung and increased the relative amount of B[a]P that was cleared by mucociliary action and subsequent ingestion. This resulted in increased absorption of B[a]P in the alimentary tract and thereby increased the dose of this compound and its metabolites to the stomach, liver, and kidneys relative to pure B[a]P.

4.2.2.2 Oral

Human. No data on the absorption of DB[a,h]A via the gastrointestinal tract in humans were identified.

Animal. Oral absorption of DB[a,h]A administered in the diet (Chang 1943) or by gavage (Chang 1943, Daniel et al. 1967) has been studied in the rat. DB[a,h]A was administered singly to rats either in the feed (250 mg) or by stomach tube (200 mg), and the amount of DB[a,h]A in rat feces was determined by a simple gravimetric method. DB[a,h]A administered in the feed or by stomach tube was slowly absorbed via the gastrointestinal tract. Recoveries of the hydrocarbon in the feces by either exposure route were in excess of 90% of the administered dose. Based upon the available literature, it is not possible to quantify the contribution of unabsorbed DB[a,h]A in the excreted material.

4.2.2.3 Dermal

Human. No data on the dermal absorption of DB[a,h]A in humans were identified. As indicated by animal data (Heidelberger and Weiss 1951), the dermal absorption rate of DB[a,h]A in humans may be anticipated to be lower than that of benzo[a]pyrene, possibly due to a slower rate of metabolism (Sanders et al. 1986, Heidelberger and Weiss 1951, Kao et al. 1985).

Animal. The dermal uptake of DB[a,h]A was studied in mice (Heidelberger and Weiss 1951). In these investigations, a single application of ^{14}C-DB[a,h]A (0.2 μmol) dissolved in benzene was applied to the shaved skin of the sacral region of mice. The sites of application were then dissected and fractionated. An average of 8% of tne applied dose was absorbed after 2 days. This rate of dermal absorption was significantly lower than that determined for benzo[a]pyrene following application of an equivalent dose (Heidelberger and Weiss 1951). Sanders et al. (1986) also found that the rate of dermal absorption of DB[a,h]A is significantly lower than that determined for B[a]P. These investigators compared the dermal penetration of [^{14}C]-B[a]P and [^{14}C]-DB[a,h]A following application to the nuchal area on the shaved backs of Swiss Webster mice. Doses of 1.25 to 125 μg/cm^2 of B[a]P in acetone were applied to 1.8 cm^2 of shaved mouse skin. Doses of 5.4, 56, and 515 μg/cm^2 of DB[a,h]A in acetone were applied to 0.2 cm^2 of shaved mouse skin. The ^{14}C contents of skin at the application site, in excreta, and in exhaled air were determined by scintillation counting. Dermal absorption of DB[a,h]A, as determined by the amount of radioactivity recovered in the tissues and excretion, was significantly lower than that determined for benzo[a]pyrene. Twenty-four hours following the maximum dose of DB[a,h]A, 67.2 ± 7.3% of the

radioactivity was recovered from the application site, 25.4 ± 8.0% from body tissues, and 7.4 ± 2.6% from excreta. Using benzo[a]pyrene under similar conditions, 17.4 ± 6.7% was recovered from the application site, 36.6 ± 10.6% from body tissues, and 46.. ± 12.3% from excreta. However, the amount absorbed did not increase as a linear function of dose, due to an apparent saturation of the uptake process. It is postulated that the difference in dermal uptake may be attributed to the lower rate of metabolism of DB[a,h]A relative to benzo[a]pyrene, since inducible enzymes such as arylhydrocarbon hydroxylase, cytochrome oxidase, and cytochrome P-450, as well as epoxide-forming enzymes, are responsible for the rapid breakdown of cutaneously deposited and absorbed PAH (Sanders et al. 1986). Results from in vitro studies (Kao et al. 1985) support the fact that cutaneous metabolism is a major factor involved in the in vitro skin permeation of surface-applied PAHs. Short-term organ cultures using mouse skin, taken from the shaved backs of mice, demonstrated that induction of cutaneous drug-metabolizing enzymes can result in a two- to threefold increase in the in vitro permeation of topical [^{14}C]-B[a]P (10 $\mu g/cm^2$ of skin).

4.2.3 Distribution

There is no quantitative information on the distribution of either inhaled or dermally absorbed DB[a,h]A.

Orally absorbed DB[a,h]A is distributed to several tissues in the rat (Daniel et al. 1967). Maximum tissue concentrations were achieved in approximately 10 h. The relative tissue affinity after 24 h was determined as: liver and kidneys > adrenals > ovaries > blood > fat. At the early stages following administration, relatively large quantities of DB[a,h]A are found in the liver and the kidneys. However, the rate of elimination from these organs is relatively rapid; after 3 to 4 days, measurable amounts of DB[a,h]A were found only in the ad. als, ovaries, and fat.

4.2.4 Metabolism

The metabolism of DB[a,h]A in human and animal systems proceeds via the biotransformation pathways established for benzo[a]pyrene [Cooper et al. 1983, Levin et al. 1982, Sims 1982, Thakker et al. 1985 (see Fig. 4.1)].

Briefly, the primary transformations are oxidation of the aromatic nucleus to form arene oxides and hydrolysis of these epoxide intermediates to *trans*-dihydrodiols in a reaction catalyzed by epoxide hydrolase (Sims and Grover 1974, Sims and Grover 1981). The dihydrodiols formed during the metabolism of DB[a,h]A are the 1,2-, 3,4-, and 5,6-dihydrodiols (MacNicoll et al. 1979). From the arene oxide precursors to the above dihydrodiols, only the 5,6-oxide (K-region oxide) has been isolated as a metabolite of DB[a,h]A (Selkirk et al. 1971, Boyland and Sims 1965). The isolation of the 3- and 4-hydroxy DB[a,h]A provided additional suggestive evidence for the formation of the 3,4-oxide (Boyland and Sims 1965).

The 3,4-dihydrodiol was metabolically activated to a biologically reactive intermediate by either microsomes or a purified monooxygenase system (Wood et al. 1978). This finding was interpreted as evidence for

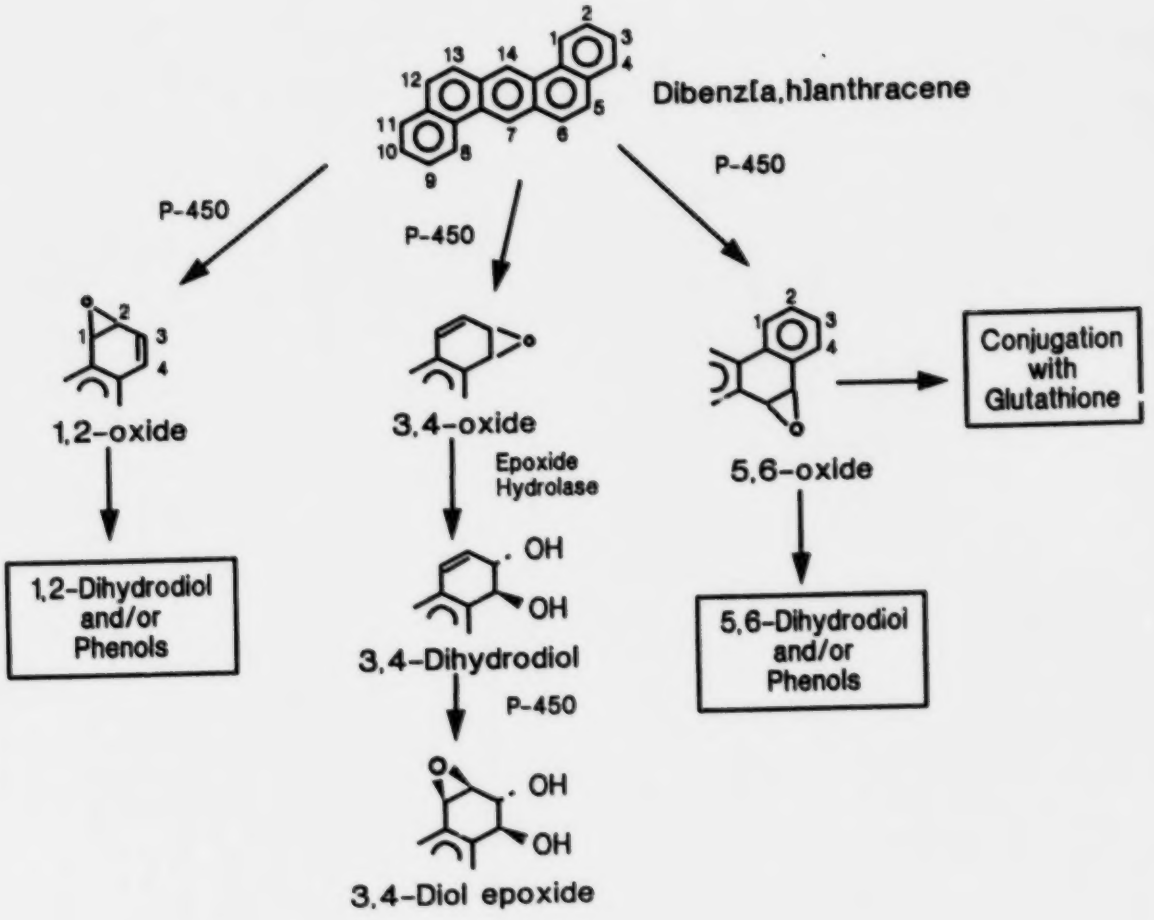


Fig. 4.1. Metabolic fate of dibenz[a,h]anthracene.

formation of a bay-region 3,4-diol-1,2-epoxide, consistent with the proposed bay-region theory of polycyclic aromatic hydrocarbon carcinogenesis (Levin et al. 1982, Thakker et al. 1985).

Other biological transformations involve conjugation of the 5,6-oxide with glutathione (Boyland and Sims 1965) and formation of sulfate and glucuronide conjugates of phenols (from nonenzymatic rearrangement of arene oxides) and *trans*-dihydrodiols (Sims and Grover 1974, Sims and Grover 1981.)

4.2.5 Excretion

The steps involved in the excretion of DB[a,h]A are likely to be those established for other polycyclic aromatic hydrocarbons. Metabolism, hepatobiliary excretion, and elimination through feces are the dominant features in this process (Schlede et al. 1970). As is the case for the other PAHs, the material excreted is expected to consist predominantly of dihydrodiol and phenol conjugates (glucuronide and sulfate esters) and glutathione conjugates.

The amount of unchanged hydrocarbon excreted in the feces by the rat, administered DB[a,h]A in the diet or by gavage, increased with the dose, suggesting saturation of metabolic pathways (Chang 1943). DB[a,h]A was eliminated by the rat predominantly in the feces (average of 90% of administered dose), and elimination was complete in approximately 2 days. The simple gravimetric technique used in this study did not allow differentiation between DB[a,h]A and its metabolites.

4.3 TOXICITY

4.3.1 Lethality and Decreased Longevity

Pertinent data regarding lethality and decreased longevity in humans or experimental animals following inhalation, oral, and dermal exposures to DB[a,h]A could not be located in the available literature.

4.3.2 Systemic/Target Organ Toxicity

No information is available on the systemic effects of DB[a,h]A in humans or experimental animals following inhalation, oral, and dermal exposures. The carcinogenic PAHs as a group cause skin disorders and have an immunosuppressive effect; however, specific results with DB[a,h]A have not been reported.

Topical application of DB[a,h]A has been reported to suppress the sebaceous glands in mouse skin (Bock and Mund 1958). Bock and Mund (1958) applied 0.2 mL of DB[a,h]A, twice daily, to two-thirds of the shaved backs of Swiss mice. Four days after the last application, mice were sacrificed. The treated skin was then subjected to an elaborate preparation and staining procedure and was qualitatively examined. DB[a,h]A was reported to suppress sebaceous glands. However, controls were not employed, and therefore it is not possible to determine if the effects seen were due to the solvent and/or the preparation procedures.

4.3.3 Reproductive and Developmental Toxicity

Pertinent data regarding the reproductive and developmental toxicity of DB[a,h]A in humans or experimental animals following inhalation, oral, and dermal exposure could not be located in the available literature. DB[a,h]A at a dose of 5 mg per rat, given subcutaneous daily from the first day of pregnancy, resulted in fetal death and resorption and may also have affected the subsequent fertility of the dams (Wolfe and Bryan 1939).

4.3.4 Genotoxicity

4.3.4.1 Overview

The genetic toxicity of DB[a,h]A has been evaluated experimentally in a variety of short-term genetic toxicology assays utilizing prokaryotes and eukaryotes as target organisms for potential genotoxic and mutagenic effects. The metabolism of DB[a,h]A is an essential event in producing these effects observed in both in vitro and in vivo biological test systems. The test systems used to evaluate DB[a,h]A's genotoxicity and the corresponding results are summarized in Tables 4.1 and 4.2.

DB[a,h]A undergoes metabolism to form several reactive intermediates. Studies have indicated that the 3,4-dihydrodiol was the most mutagenic to bacteria in the presence of rat-liver preparations (Wood et al. 1978). The 5,6-oxide metabolite (Selkirk et al. 1971) transformed hamster embryo cells at a higher rate than the parent compound (Huberman et al. 1972, Grover et al. 1971). The 3,4-dihydrodiol of DB[a,h]A is thought to be metabolized to a 3,4-diol-1,2-epoxide, the reactive, ultimately mutagenic, metabolite. These reactive electrophiles are capable of interacting and binding to the DNA to form bulky DNA adducts that are generally regarded as an important determinant in mutagenesis and clastogenesis (Brendel and Ruhland 1984). The genotoxicity of DB[a,h]A is dependent on metabolic activation, either exogenously supplied or endogenously present, and the ratio of enzymatic activation and detoxication pathways.

4.3.4.2 General discussion

The genotoxicity of DB[a,h]A has been demonstrated in various in vitro genetic assays. DB[a,h]A was positive in in vitro differential survival assays measuring DNA damage that used DNA-repair-proficient/deficient strains of bacteria. Unscheduled DNA synthesis was observed in both human epithelial and HeLa cell cultures, but none were noted in rodent cell cultures. DB[a,h]A was mutagenic in *Salmonella typhimurium* and cultured mammalian cells in the presence of an exogenous metabolic activation system. Generally, it was positive in rodent cell transformation assays. Only one study showed that it was mutagenic to a human epithelial-like cell line.

In the only available cytogenetic study in vivo, DB[a,h]A exposure resulted in a weak induction of SCEs, but no induction of chromosomal aberrations in Chinese hamster bone marrow cells (Roszinsky-Kocher et al. 1979). The only heritable gene mutation study available was by

Table 4.1. Genetic toxicity of dibenz[a,h]anthracene (in vitro)

End points	Species (test systems)	Results with or without activation[a]	References
DNA damage	*Escherichia coli* (rec+/rec-)	Positive - activation	Ichinotsubo et al. 1977
	Bacillus subtilis (rec+/rec-)	Positive - activation	McCarroll et al. 1981
DNA damage (UDS)	Syrian hamster embryo cells	Negative - no activation	Casto et al. 1976
	Primary rat hepatocytes	Negative - no activation	Probst et al. 1981
	Rat tracheal epithelial cells	Negative - no activation	Ide et al. 1981
	HeLa cells	Positive - activation	Martin et al. 1978
	Human foreskin epithelial cells	Positive - no activation	Lake et al. 1978
Gene mutations	*Neurospora crassa* (reverse mutation)	Negative - no activation	Burdette and Haddox 1954
	Neurospora crassa (forward mutation)	Positive - no activation	Barratt and Tatam 1958
	Salmonella typhimurium TA100 (his+/his-)	Positive - activation	Levitt et al. 1979, Baker et al. 1980, McCann et al. 1975, Wood et al. 1978
	Salmonella typhimurium TM677 (8AGs/8AGr)	Positive - activation	Kaden et al. 1979
	Chinese hamster V79/HGPRT (6-TG)	Positive - activation	Krahn and Heidelberger 1977, Diamond et al. 1984
	V79/Na+,K+ATPase	Positive - activation	Huberman and Sachs 1976
	V79/APRT (8-AG)	Positive - activation	Huberman and Sachs 1976
	Mouse lymphoma L5178Y/TK+/-	Positive - activation	Thornton et al. 1982
	Human EUE epithelial-like cells (diptheria toxin)	Positive - activation	Rocchi et al. 1980

Table 4.1. (continued)

End points	Species (test systems)	Results with or without activation[a]	References
Sister chromatid exchange (SCE)	Chinese hamster ovary cells	Negative - no activation	Pal 1981
Chromosomal aberrations	Primary rat cells	Positive - no activation	Kislova 1972
Cell transformation	Syrian hamster embryo cells (clonal assay)	Positive - no activation	DiPaolo et al. 1969, Pienta et al. 1977, Huberman et al 1972
	Syrian hamster embryo cells (focal assay)	Positive - no activation	Casto et al. 1977
	Mouse C3H/10T1/2 cells	Positive - no activation	Reznikoff et al. 1973
	Mouse C3H/10T1/2 cells	Negative - no activation	Lubet et al. 1983
	Mouse prostate C3H cells	Positive - no activation	Chen and Heidelberger 1969
	Mouse prostate C3HG23 cells	Negative - no activation	Marquardt et al. 1972
	RLV/Fischer rat embryo cells	Positive - no activation	Freeman et al. 1973
	Mouse BALB-C3T3 cells	Positive - no activation	Sivak et al. 1980
	AKR/mouse embryo cells	Positive - no activation	Rhim et al. 1974
	SA7/Syrian hamster embryo cell	Positive - no activation	Casto 1973, Casto et al. 1973
	SA7/rat embryo cell	Positive - no activation	DiPaola and Casto 1976

[a]The results presented in Tables 4.1 and 4.2 are based on the activity profiles prepared by Waters et al. (1987), Gene-Tox listings supplied by John S. Wassom, and/or personal review of the original citations.

Table 4.2. Genetic toxicity of dibenz[a,h]anthracene (in vivo)

End points	Species (test systems)	Results[a]	References
Sister chromatid exchange	Chinese hamster bone marrow cells	Positive	Roszinsky-Kocher et al. 1979
Chromosomal aberrations	Chinese hamster bone marrow cells	Negative	Roszinsky-Kocher et al. 1979
Gene mutations	*Drosophila melanogaster* (sex-linked recessive lethal)	Positive	Demerec 1948

[a]The results presented in Tables 4.1 and 4.2 are based on the activity profiles prepared by Waters et al. (1987), Gene-Tox listings supplied by John S. Wassom, and/or personal review of the original citations.

Demerec (1948) who reported positive results in *Drosophila melanogaster* sex-linked lethal test via inhalation.

There is sufficient evidence from mostly in vitro assays to indicate that DB[a,h]A is a genotoxic agent when metabolically activated to the dihydrodiol and oxide forms. However, the absence of information on the ability of DB[a,h]A to reach and interact with mammalian germ cells makes it difficult to state whether this chemical is genotoxic in humans.

4.3.5 Carcinogenicity

4.3.5.1 Overview

The carcinogenicity of DB[a,h]A has not been adequately studied. There are no reports directly correlating human DB[a,h]A exposure and tumor development, although humans are likely to be exposed by all routes. There are a number of reports associating human cancer and exposure to mixtures of PAHs that include DB[a,h]A, however. There is experimental evidence that DB[a,h]A can cause tumors in mice following oral administration and lung tumors in rats and hamsters following intratracheal instillation, and that it is a skin carcinogen following dermal application; in fact, DB[a,h]A was the first chemically pure substance shown to induce cancer (Kennaway and Heiger 1930). It is likely that DB[a,h]A could cause cancer in humans as well.

4.3.5.2 Inhalation

Human. No studies on the carcinogenicity of DB[a,h]A in humans following inhalation exposure were found in the available literature. However, epidemiologic studies have shown an increased incidence of lung cancer in humans exposed to coke oven emissions (Lloyd 1971, Redmond et al. 1972, Mazumdar et al. 1975), roofing tar emissions (Hammond et al. 1976), and cigarette smoke (Wynder and Hoffmann 1967, Maclure and MacMahon 1980, Schottenfeld and Fraumeni 1982). Each of these mixtures contains DB[a,h]A as well as other carcinogenic PAHs and other potentially carcinogenic chemicals such as nitrosamines. It is thus impossible to evaluate the contribution of DB[a,h]A to the total carcinogenicity in humans of these mixtures due to their complexity and the presence of other carcinogens. Reports of this nature provide a qualitative suggestion of the potential for DB[a,h]A-induced carcinogenicity nonetheless.

Animal. No studies on the carcinogenicity of DB[a,h]A in animals following inhalation exposure were found in the available literature. DB[a,h]A has been shown to be a lung carcinogen following intratracheal instillation, however. Sellakumar and Shubik (1974) administered DB[a,h]A and hematite in saline suspension to male Syrian golden hamsters. Groups of 48 animals received 24 and 30 doses at weekly intervals of 0.05 or 0.25 mg DB[a,h]A, respectively, and were allowed to die spontaneously or were killed when moribund. No respiratory tract tumors were found in the low-dose group, while 2/46 animals with respiratory tract adenocarcinomas were seen in the high-dose group. No respiratory tract tumors were found among 82 untreated controls. In another experiment, a total of 170 "mongrel albino" rats received five

intratracheal instillations of DB[a,h]A in suspension with protein blood substitute and india ink (Yanysheva and Balenko 1966). Animals received total doses of 0, 0.5, 2, 10, or 20 mg DB[a,h]A and were observed for 30 months. Squamous cell carcinomas were observed in 0/15, 0/18, 1/27, 4/21, and 6/13 animals, respectively. These experiments indicate that DB[a,h]A is a weak to moderately potent respiratory tract carcinogen.

4.3.5.3 Oral

Human. No studies on the carcinogenicity of DB[a,h]A in humans following oral exposure were found in the available literature.

Animal. Several studies concerning the carcinogenicity of DB[a,h]A in animals following oral exposure via the diet or drinking water were available. In three studies, mice of various strains received 0.16 or 0.20 mg DB[a,h]A per milliliter aqueous mineral oil or olive oil emulsions in place of drinking water throughout their lifetimes (Lorenz and Stewart 1948; Snell and Stewart 1962, 1963). Lung adenomas and forestomach papillomas and squamous cell carcinomas were observed; however, extensive dehydration and emaciation occurred since animals did not tolerate the vehicle well, leading to early death and the need to remove the animals from the treatment vehicle periodically. Mammary carcinoma was observed in 1/20 female BALB/c mice that received twice weekly treatments with 0.5% DB[a,h]A in almond oil by gavage for a total dose of 15 mg/animal after 15 weeks; however, no control group was included (Biancifiori and Caschera 1962). Mice (strain unspecified) receiving DB[a,h]A in the diet for 5 to 7 months for total doses of 9 to 19 mg developed forestomach tumors in 7/22 animals surviving at 1 year (Larinow and Sobioliva 1938). None of these studies was adequately reported; they did not include appropriate histopathology, adequate treatment or study durations, or large enough sample sizes. As a result, they were judged inadequate by contemporary standards to support the development of significant human exposure levels for carcinogenicity, although they provide some evidence of DB[a,h]A's carcinogenicity by the oral route.

4.3.5.4 Dermal

Human. No studies on the carcinogenicity of DB[a,h]A in humans following dermal exposure were found in the available literature. As with inhalation exposure, however, there are reports of skin cancer among individuals exposed dermally to mixtures of PAHs containing DB[a,h]A. The earliest of these is the report of Pott (1775) of scrotal cancer among chimney sweeps. More recently, skin cancer among those exposed dermally to shale oils has been reported (Purde and Etlin 1980). These reports provide only qualitative suggestions of the carcinogenic potential of DB[a,h]A in humans, however, due to the presence of other putative carcinogens in the mixtures.

Animal. DB[a,h]A has been shown to cause skin tumors in mice following dermal application. The results of a key study by Wynder and Hoffmann (1959) are shown in Table 4.3. As part of a study of the carcinogenicity of tobacco and its constituents, these authors tested several PAHs, including DB[a,h]A, as carcinogens on mouse skin. Groups of 20 female Swiss mice received concentrations of 0.001, 0.01, or 0.1%

Table 4.3. Carcinogenic activity of dibenz[a,h]anthracene on mouse skin

Source	Dose[a] (% concentration)	Tumor incidence	
		Papillomas	Carcinomas
Wynder and Hoffmann 1959	0.001	6/15 (40)[b]	6/15 (40)
	0.01	19/20 (95)	18/20 (90)
	0.1	18/19 (95)	15/19 (78)
Van Duuren et al. 1967	0.001	1/30 (3)	1/30 (3)
	0.01	43/50 (86)	39/50 (78)
	0.1	39/40 (98)	32/40 (80)
	0	0/120 (0)	0/120 (0)

[a]In these experiments, female Swiss mice received doses of DB[a,h]A in acetone applied to their backs with a brush three times weekly throughout their lives.

[b]Data within parentheses indicate percentages.

DB[a,h]A dissolved in acetone three times a week applied to their backs with a brush throughout their lifetimes. No solvent control group was reported; however, since no papillomas or carcinomas were obtained for several of the PAHs tested, a solvent control group would most likely have been negative as well. Incidences of papillomas and carcinomas at the site of application were dose related at the two lowest doses. The decrease in tumor rate at the highest dose tested probably reflects DB[a,h]A's toxicity and the resulting decreased survival observed. Reductions in tumor latency period were also found to be dose related.

In another study, Van Duuren et al. (1967) employed a protocol identical to that of Wynder and Hoffmann (1959), but using from 30 to 50 animals per group, and obtained the results also shown in Table 4.3. Dose-related increases in both papilloma and carcinoma formation, as well as decreased survival time and tumor latency period, were observed.

Dose-response relationships for the dermal carcinogenicity of DB[a,h]A have thus been demonstrated over a 2 order-of-magnitude dose range. The lowest concentration at which DB[a,h]A elicited tumors was 0.001%, which is approximately equal to a dose of 2.9×10^{-2} mg/kg (1.2×10^{-2} mg/kg/day).

The potential of DB[a,h]A to initiate skin tumor formation has also been demonstrated using a standard initiation/promotion protocol (IARC 1973).

4.3.5.5 General discussion

The only end points of toxicity using relevant human exposure routes that have been evaluated for DB[a,h]A are that of dermal and oral carcinogenicity. DB[a,h]A has also been shown to elicit tumors following subcutaneous or intramuscular injection in rats, mice, guinea pigs, and birds, and in rats and hamsters following intratracheal administration with india ink or hematite (IARC 1973, Sellakumar and Shubik 1974). The mechanism of DB[a,h]A-induced carcinogenicity is likely to be similar to that of other PAHs; namely, involving metabolic activation to reactive diol epoxide derivatives that can form adducts with DNA which lead to mutation and tumor initiation under certain circumstances.

4.4 INTERACTIONS WITH OTHER CHEMICALS

Most human exposures to DB[a,h]A are not to the pure compound but to particle-bound DB[a,h]A; the presence of particles is likely to affect its pharmacokinetics and carcinogenicity. Sun et al. (1982) showed that when the carcinogenic polycyclic aromatic hydrocarbon benzo[a]pyrene was particle-bound, it was cleared from hamster lungs much more slowly than a pure B[a]P aerosol, thus increasing the length of time the lungs were exposed and increasing the dose to the gastrointestinal tract as a result of mucociliary clearance. Respirable PAH-containing particulates such as diesel exhaust, when coated with the phospholipid component of a pulmonary surfactant, are genotoxic (Wallace et al. 1987). Dusts can increase the rates of pulmonary cell proliferation (Harris et al. 1971, Stenback et al. 1976, Stenback and Rowland 1979), which in turn increases the susceptibility of those cells to an initiation event in the presence of a carcinogen. Coadminis' ation of B[a]P and particles greatly increases respiratory tract tumor yields

in experimental animals (Stenback et al. 1976, Stenback and Rowland 1979). The effects of particles on potential DB[a,h]A carcinogenesis is likely to be similar.

Human exposure to DB[a,h]A in the environment seldom, if ever, occurs to DB[a,h]A alone but to DB[a,h]A as a component of complex mixtures of PAHs and other chemicals. Interactions between DB[a,h]A and other mixture components are likely to occur. In particular, interactions may play a large part in carcinogenesis resulting from experimental exposure to PAHs. For example, Mahlum et al. (1984) have shown that different temperature range distillates of coal liquids have different skin-tumor-initiating activities in mice despite the fact that they contain similar levels of known carcinogenic PAHs. This difference is believed to be due to the modifying effects of the spectrum of noncarcinogenic PAHs obtained at different temperatures. Most of the PAH components of coal liquid fractions obtained at different temperatures will vary both qualitatively and quantitatively, and consequently their abilities to modify carcinogenesis will vary accordingly. The relative roles of the PAH components of each of such mixtures are unknown, however, so that quantitative evaluation is not possible. Since human exposure occurs to mixtures of PAHs, and not individual components, quantitative evaluation of the toxicity of individual PAHs is probably insufficient.

Human exposure to complex mixtures of PAHs has been extensive, and some adverse effects are well documented, particularly carcinogenic effects following long-term exposure. The extent of human exposures to well-defined PAH mixtures that are responsible for producing excess disease is generally not known in quantitative terms. Coke oven emissions and related substances such as coal tar have probably been the most widely studied. Coal tar derivatives were most likely responsible for the first observation of occupational cancer, that of scrotal cancer among London chimney sweeps, made by Percival Pott in 1775. More recent mortality studies have demonstrated strong associations between human exposure to coke oven emissions and excess disease; specifically, significant increases in lung and genitourinary cancer mortality have been observed (IARC 1983). The earliest of these reports was made in 1936 by investigators in Japan and England (Kennaway and Kennaway 1936) who were studying lung cancer mortality among persons employed in coal carbonization and gasification processes. Subsequent studies conducted in the United States clearly demonstrated substantial increases in lung and genitourinary system cancer mortality among coke oven workers (Lloyd 1971, Redmond et al. 1972, IARC 1984). Human tumorigenicity has also been reported to result from exposure to creosote. Creosote is a generic term that refers to wood preservatives derived from coal tar, creosote, or coal tar neutral oil, and includes extremely complex mixtures of liquid and solid aromatic hydrocarbons. Workers who engaged in activities such as dipping timbers in creosote were reported to have developed malignant and premalignant skin lesions of the face, arms, and scrotum (O'Donovan 1920, Cookson 1924, Henry 1947, Lenson 1956). Many of the individual PAH components of creosote, such as DB[a,h]A, have been shown to be both mutagenic and carcinogenic in laboratory bioassays, supporting the evidence of its human carcinogenicity (IARC 1983).

Exposures to many other complex chemical mixtures that include PAHs have been associated with human disease incidence, such as the use of tobacco products and exposure to roofing tar emissions and shale oils. Although this discussion falls short of providing a thorough review of the extensive literature available on the experimental and epidemiological observations of the toxicity of PAH mixtures, its purpose has been to provide examples wherein such toxicity has been documented in order to emphasize that human exposure occurs to multiple PAHs.

Predicting the toxicity of a complex mixture on the basis of one or several of its components may be misleading due to the possibility of interactions among the components that may modify toxicity. For example, both carcinogenic and noncarcinogenic PAHs may compete for the same metabolic activating enzymes and thereby reduce the toxicity of carcinogenic PAHs. Steiner and Falk (1951) showed that simultaneous administration of DB[a,h]A and benz[a]anthracene by subcutaneous injection in mice inhibited DB[a,h]A's carcinogenicity. Exposure to other PAHs may induce enzyme levels leading to more rapid detoxication of DB[a,h]A, reducing its carcinogenicity (Slaga and diGiovanni 1984, Weibel 1980). Naturally occurring compounds have been found to induce the enzymes that metabolize PAHs, leading to either increased or decreased toxicity. For example, plant flavonoids can induce microsomal monooxygenases and reduce the carcinogenicity of DB[a,h]A (Weibel 1980). Environmental contaminants such as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) can also increase microsomal enzyme activity and consequently affect PAH toxicity (Kouri et al. 1978). Interactions can thus play important modulating roles in PAH toxicity that may not be adequately reflected in the identification of significant human exposure levels based on the toxicity of single PAHs since human exposure occurs to mixtures of PAHs.

5. MANUFACTURE, IMPORT, USE, AND DISPOSAL

5.1 OVERVIEW

DB[a,h]A is on the Toxic Substances Control Act (TSCA) Chemical Inventory (EPA 1979a) which lists chemicals (as defined by TSCA) that have been manufactured, imported, or processed for a commercial purpose in the United States since January 1, 1975. DB[a,h]A is found in fossil fuels and as a result of the incomplete combustion of fuel and wood. DB[a,h]A is also available as a research chemical by some specialty chemical suppliers. DB[a,h]A and other PAHs are found in coal tar and in the creosote oils and pitches formed from the distillation of coal tars. Coal tar pitch is primarily used as a binder for electrodes. Creosote is primarily used as a wood preservative. Coal tar is also used as a therapeutical treatment for skin diseases such as psoriasis. PAHs are also found in small amounts in bitumens and asphalt used in paving and for industrial use.

5.2 PRODUCTION

The primary source of DB[a,h]A in air is the incomplete combustion of fuel or wood for heating (EPA 1985).

Crude coal tar is produced as a by-product in the formation of coke from coal. Hot gases and vapors that are released from the conversion of coal to coke are collected in a scrubber that condenses these gases into ammonia, water, crude tar, and other by-products. A typical coke oven produces 80% coke, 12% coke-oven gas, 3% coal tar, and 1% crude benzene. The coal tar is then distilled to yield a number of chemical oils, creosote, and coal tar pitch. The coal tar pitch residue is 40.5% of the crude tar; creosote is approximately 11.5%. Heavy and light creosote also make up a small percentage of distillate (NIOSH 1977). High-temperature coal tar contains 0.1% DB[a,h]A (IARC 1985). Creosote contains approximately 0.01 to 0.04% DB[a,h]A (IARC 1985).

As of 1981, the world output of crude coal tar was 18×10^6 t; 14×10^6 t were of coke-oven origin. In 1980, the United States production of crude tar was 2.4×10^6 t. Creosote oil production in the United States in 1981 was estimated to be 0.51×10^6 t. The coal tar pitch production in the United States in 1974 was estimated to be 1×10^6 t (McNeil 1983).

5.3 IMPORT

In 1985, the United States imported a total of almost 12 million gallons of creosote oil from the Netherlands, France, West Germany, and other countries and almost 185 million pounds of coal tar pitch, blast furnace tar, and oil-gas tar from Canada, Mexico, West Germany, Asian countries, Australia, and other countries (USDOC 1986).

5.4 USE

DB[a,h]A has some use as a research chemical. It is available from some specialty chemical suppliers in low quantities (100 to 500 mg) (Aldrich Chemical Co. 1986).

Coal tar pitch is primarily used as a binder for electrodes in the aluminum reduction process; it is used to bind the carbon electrodes used in the reduction pots (NIOSH 1977). In North America, coal tar pitch is also used as the adhesive in membrane roofs (McNeil 1983).

Almost 99% of creosote produced is sold to wood preservation plants; 0.1 to 0.2% is sold to individual customers (NIOSH 1977). Creosote is used in the preservation of railroad ties, marine pilings, and telephone and telegraph poles. Some creosote is also consumed as fuel by steel producers (NIOSH 1977).

Coal tar is also used in the clinical treatment of skin disorders such as eczema, dermatitis, and psoriasis. The use of dermatological coal tar preparations is extensive (NIOSH 1977).

Bitumens and asphalt (a mixture of bitumens and mineral material) are used for road paving and in industry for sound- and waterproofing and pipe coating (IARC 1985).

5.5 DISPOSAL

No information concerning the disposal of DB[a,h]A was located in the available literature.

6. ENVIRONMENTAL FATE

6.1 OVERVIEW

DB[a,h]A in the environment is derived from both natural (e.g., wildfires and volcanoes) and man-made sources, but DB[a,h]A originating from man-made sources is by far quantitatively the most significant. DB[a,h]A, like all PAHs, is formed during high-temperature pyrolytic processes. Consequently, combustion is the major source of environmental DB[a,h]A. All direct releases of DB[a,h]A into the environment are to the air. DB[a,h]A is removed from the atmosphere by photochemical oxidation and dry or wet deposition to land or water. DB[a,h]A that reaches the surface will likely remain and will be partitioned primarily to soil/sediment, where it is very persistent. The dominant degradation process for DB[a,h]A in soil/sediment is biodegradation. Biodegradation is a slow process; a half-life of 750 days has been reported for DB[a,h]A in soil.

6.2 RELEASES TO THE ENVIRONMENT

Incomplete combustion of carbonaceous material is the major source of PAHs and thereby DB[a,h]A formation in the environment. Residential heating is the largest combustion source of DB[a,h]A. The large quantity of DB[a,h]A released by this source is a consequence of inefficient combustion processes and uncontrolled emissions. In a recent assessment of DB[a,h]A sources and release volumes across the United States, EPA (1985) estimated that home coal combustion contributed 30 t, or 67% of all released volumes. Home heating with wood was estimated to contribute 11 t, or 25% of DB[a,h]A releases. Publicly owned treatment works (POTWs) also release approximately 4 t of DB[a,h]A into the atmosphere. Small amounts of DB[a,h,]A are likely formed and released into the environment during coal tar production and use and during gasoline and diesel fuel combustion. Also PAH-containing products such as creosote-treated wood and asphalt roads may release small amounts of DB[a,h]A and other PAHs into the environment.

Although exposure levels are not yet quantified on a national basis, waste sites may be an additional source of environmental DB[a,h]A. For example, abandoned wood treatment plants are sources of high concentrations of creosote, and former manufactured gas plants (town gas sites) are sources of high concentrations of coal tar. Both creosote and coal tar are composed of a variety of PAHs, including DB[a,h]A. PAHs at these sites are likely to occur on the soil and on suspended particulate matter in the air.

6.3 ENVIRONMENTAL FATE

Few data are available which describe the environmental fate of DB[a,h]A, specifically. Much of the understanding of DB[a,h]A fate is based upon analogy to benzo[a]pyrene, benz[a]anthracene, and PAHs in general. The discussion below is based primarily on these generalizations.

The environmental fate of PAHs, such as DB[a,h]A, is determined to a large degree by the chemical's low water solubility and high propensity for binding to particulate or organic matter. As a result, DB[a,h]A in the atmosphere is expected to be associated primarily with particulate matter, especially soot, whereas the majority of DB[a,h]A in aquatic systems is expected to be strongly bound to suspended particles or bed sediments. Likewise, DB[a,h]A will be strongly sorbed to surface soils. Dispersion of particle-bound DB[a,h]A is the primary transport process within air, water, and land. DB[a,h]A can leach through soils, but a low water solubility will most likely limit the relative importance of this intramedium transport process.

Based upon an analogy to benzo[a]pyrene, dry deposition of particle-bound DB[a,h]A is probably the most significant transport process between air and land or water (EPA 1979b), although wet deposition of DB[a,h]A is known to occur (VanNoort and Wondergem 1985). Because of a very low vapor pressure, DB[a,h]A that reaches the surface will likely remain and will be partitioned primarily to soil/sediment. Soil/particle adsorption or biotic uptake are the primary transport processes for the removal of waterborne DB[a,h]A. Desorption into water from soil is very unlikely, and erosion of contaminated soils by surface runoff is the most probable transport process for soil-bound DB[a,h]A to aquatic systems.

Information about the fate of particulate PAHs, including DB[a,h]A, released to the atmosphere is presently unclear. It is generally assumed, however, that photochemical oxidation processes play an important role. Atmospheric half-lives on the order of days have been suggested (NAS 1972). PAHs strongly absorb solar radiation at wavelengths above 300 nm, and there is sufficient evidence to indicate that PAHs undergo photooxidation in solution, as pure solids, and when adsorbed onto certain solid substrates such as alumina (NAS 1972). Singlet oxygen has been implicated as the primary oxidant, and endoperoxides and, ultimately, quinones as the reaction products (NAS 1972).

It has been inferred that similar processes take place when the compounds are adsorbed on airborne particles. Kamens et al. (1986) reported that PAHs adsorbed on soot particles rapidly decayed in the presence of sunlight. However, photooxidation of these same compounds adsorbed on carbon black particles was extremely slow (Barofsky and Baum 1976). Similarly, Korfmacher et al. (1980a,b) found that benzo[a]pyrene and other PAHs that are adsorbed on fly ash are highly resistant to photodegradation. More research is needed to elucidate the rate and substrate dependency of atmospheric PAH degradation.

Data collected by Smith et al. (1978) indicate that within aquatic systems, most PAHs accumulate in the sediment and are transported with

suspended sediment. PAHs in the water column also accumulate in aquatic organisms. However, many organisms metabolize and excrete PAHs rapidly so that bioaccumulation is a short-term process. For example, in bluegill sunfish, an 89% loss of benzo[a]pyrene (B[a]P) was recorded 4 h after exposure (Leversee et al. 1981). Lee et al. (1972) reported rapid elimination of B[a]P in three species of California marine teleosts. Depuration rates in invertebrate species vary more widely. Some species, such as hard-shell clams, show little or no depuration, while others, such as oysters, eliminate virtually all PAHs following exposure (Eisler 1987).

Aquatic organisms also can assimilate PAHs from food. For example, crustaceans and fish have been reported to readily assimilate PAHs from contaminated food (Eisler 1987). However, in many cases where assimilation of PAHs has been demonstrated, metabolism and excretion of PAHs were rapid (Eisler 1987). In laboratory aquatic ecosystem studies in which radiolabeled B[a]P was used, Lu et al. (1977) found that B[a]P can be accumulated through the food to high levels in mosquito fish. After 3 days of exposure, the intact parent compound accounted for over 50% of the extractable radiolabeled carbon in fish. However, after 33 days of exposure, the intact parent compound accounted for only 7% of the total extractable radiolabeled carbon, indicating metabolism of B[a]P. The tendency of fish to metabolize B[a]P and other PAHs may explain why these compounds are frequently undetected, or only detected in low concentrations in the livers of fish from environments heavily contaminated with PAHs.

A minimal amount of PAHs is dissolved in the water column and degraded rapidly (half-life is several hours) (EPA 1979b) by direct photolysis. Chemical oxidation may be a significant fate process for DB[a,h]A in the water when chlorine or ozone (both oxidants) exist in sufficient concentrations (EPA 1979b).

The major fate of sediment-bound PAHs, including DB[a,h]A, however, is most likely biodegradation (EPA 1979b). In general, the biodegradation processes are quite slow; a half-life of 7,000 h has been reported for benzo[a]anthracene (EPA 1979b), and it is likely that the biodegradation rate for DB[a,h]A is similar. Biodegradation half-lives in contaminated streams can be 10 to 400 times longer. These long half-lives indicate that PAHs are relatively persistent in sediments and aquatic systems.

Within terrestrial systems, biodegradation also is the probable primary fate process. However, this process is very slow. As a result, DB[a,h]A is very persistent in soils. Coover and Sims (1987) estimated a half-life of DB[a,h]A in soil of 750 days.

At hazardous waste sites, half-lives may be longer as other contaminants present at the site may be toxic to the degrading microorganism. Bossert and Bartha (1986) reported reduced biodegradation of PAHs in soil containing a chemical toxic to microorganisms.

7. POTENTIAL FOR HUMAN EXPOSURE

7.1 OVERVIEW

As the previous discussions indicate, virtually all estimated environmental DB[a,h]A releases are part of releases of mixtures of PAHs and are emitted directly into the atmosphere. Consequently, inhalation is one of the primary routes of background human exposure to DB[a,h]A in the environment. Part of the DB[a,h]A in the atmosphere returns to the surface via dry and wet deposition. This input leads to DB[a,h]A in soil and water to which humans may be exposed. Background exposures to DB[a,h]A are expected to be at very low levels. Much higher exposure concentrations are associated with tobacco smoke and certain occupational exposures. Humans also may be exposed to DB[a,h]A in food, tobacco smoke, and certain occupational settings, and through contact with PAH-containing products such as coal tar, asphalt, and creosote-treated wood. At hazardous waste sites, humans most likely will be exposed to DB[a,h]A in the soil and on particulate matter in the air. At this time, DB[a,h]A has been found at 16 of the 1,177 hazardous waste sites on the National Priorities List (NPL) in the United States (View 1989).

7.2 LEVELS MONITORED IN THE ENVIRONMENT

7.2.1 Air

No studies have been conducted in which atmospheric levels of DB[a,h]A were monitored in U.S. cities. However, DB[a,h]A is released directly into the air during certain combustion processes, and, therefore, it is likely that the substance exists to some degree in the atmosphere. Ambient levels of DB[a,h]A are expected to be lower than the ambient concentrations of other PAHs because atmospheric release volumes are 3 to 20 times less than those of other PAHs (EPA 1985).

7.2.2 Water

DB[a,h]A has been detected at low concentrations (<2 ng/L) in raw and finished drinking waters in the United States (Sorrell et al. 1981), but minimal data limit the degree to which background levels can be adequately characterized. Because of a high propensity to bind to organic matter, it is unlikely that DB[a,h]A will occur to any appreciable extent in surface water or groundwater at hazardous waste sites or other areas.

7.2.3 Soil

No data are available on DB[a,h]A levels in U.S. soils. But Blumer et al. (1977) summarized data on total PAH levels in soil and reported

concentrations of between 4 and 13 mg/kg in the soil from relatively rural areas of the eastern United States. PAH levels in soils in more populated and industrialized areas may be higher. Butler et al. (1984) examined soil PAH levels in Switzerland and demonstrated much higher soil DB[a,h]A concentrations near complex road interchanges than at areas more distant. Also, the soils at waste sites, such as former manufactured gas sites and creosote wood treatment plants, can be expected to contain high levels of PAHs, including DB[a,h]A.

7.2.4 Food

Data on DB[a,h]A levels in food are limited, primarily because the substance is not one of the PAHs commonly analyzed in food. However, DB[a,h]A has been detected in vegetables (0.5 to 2.6 μg/kg) and edible oils (0 to 1.9 μg/kg) (IARC 1983). DB[a,h]A also has been detected in charcoal broiled steaks at a level of 0.2 μg/kg (Lijinsky and Shubik 1964). The amount of DB[a,h]A in meat depends upon the method of cooking; time of exposure, distance from the heat source, and the disposal of fat during cooking all influence DB[a,h]A content.

DB[a,h]A has been detected in vegetables and fruits grown in PAH-contaminated soil near high traffic areas (Wang and Meresz 1982). PAHs also have been detected in fruits and vegetables grown in contaminated air (Grimmer 1979). Thus consumption of food grown in contaminated soil or air, which may occur near hazardous waste sites, industrial areas, or highways, may contribute to human exposure.

Humans also may be exposed to PAHs, including DB[a,h]A, in aquatic organisms such as fish, clams, and oysters that are typical components of the diet. PAHs have been detected in bivalve mollusks (e.g., clams, oysters, and mussels), crabs, and lobsters (Eisler 1987). PAHs also have been detected in fish, but fish levels are usually low, probably because this group rapidly metabolizes PAHs.

7.2.5 Tobacco Smoke

DB[a,h]A has been reported to occur in cigarette mainstream smoke at a level of 4 ng/cigarette (IARC 1983). Concentrations in side-stream smoke may potentially be higher, since levels between 2 to 4 times higher have been reported for other PAHs (DHHS 1986). Thus, passive smokers, in addition to smokers, may receive elevated exposures to DB[a,h]A from cigarettes.

7.3 OCCUPATIONAL EXPOSURES

PAHs, such as DB[a,h]A, have been isolated in numerous occupational situations, including coal tar production and coking plants, coal-gasification sites, smoke houses, aluminum production plants, bitumen and asphalt production plants, coal tarring activities, and around municipal incinerators. Historically, the highest level of human exposure to PAHs occurred in industrial situations. Concentrations of benzo[a]pyrene, often used as an indicator of total PAH concentration, have been reported to range from 800 to 23,100 ng/m^3 in the workroom air of coke oven operations in the United Kingdom (Davies et al. 1986). Similarly high values have been reported by Lindstedt and Sollenberg (1982) in Swedish industries.

7.4 POPULATIONS AT HIGH RISK

At highest risk for cancer by PAHs, such as DB[a,h]A, are those people who are exposed to high levels of PAHs. Examples of high-risk populations include workers in certain occupations that have elevated PAH concentrations in the ambient work environment; tobacco smokers and involuntary (passive) smokers who receive elevated PAH intake in tobacco smoke; and populations living near industries (such as creosote and coal tar manufacturers) that generate PAHs as a by-product of production.

Individuals in these high-exposure groups may have varying susceptibilities to PAH toxicity. Some of the available data on PAH carcinogenicity suggest a relationship between aryl hydrocarbon hydroxylase (AHH) activity and cancer risk. Genetic variation in AHH inducibility has been implicated as a determining factor for susceptibility to lung and laryngeal cancer (EPA 1980). Attempts have been made to demonstrate that persons with lung cancer have higher inducibility of AHH in cultured lymphocytes. A review by Calabrese (1984) indicates that several studies support this hypothesis, and some genetic data indicate that the human population can be segregated based upon this trait (EPA 1980). Thus, individuals that are AHH-inducible may constitute a special risk population. However, the data regarding genetic susceptibility are not conclusive.

8. ANALYTICAL METHODS

8.1 ENVIRONMENTAL SAMPLES

The procedures used to sample and extract DB[a,h]A in different media are very similar. In air and tobacco smoke, polycyclic aromatic hydrocarbons, including DB[a,h]A, are adsorbed predominantly on particulate matter, and the particulate matter is collected on a filter. In water and soil, PAHs are extracted without filtration.

The extraction of PAHs from the filter can be accomplished by a variety of techniques with or without solvents. The following extraction methods are the most commonly used techniques: soxhlet, sublimation at elevated temperatures, ultrasonic, and polytron extraction (Sawicki 1976).

A cleanup step is necessary to separate DB[a,h]A and PAHs from other extracted substances. Typically, this step involves liquid-liquid extraction of the dry organic particulate extract followed by adsorption chromatography using silica gel or alumina columns (Sawicki 1976, Riggin and Strup 1984). These adsorbents selectively remove interfering compounds. In addition, thin-layer chromatography can be used as a cleanup method (Sawicki 1976).

The most commonly used analytical methods for determining DB[a,h]A in environmental samples are column gas chromatography (GC) and high-performance liquid chromatography (HPLC). Table 8.1 summarizes common analytical methods, detection limits, and accuracy (percent recovery) for the determination of DB[a,h]A in air, water, soil, and food.

Column gas chromatography is an analytical technique in which components of a sample are separated by differential distribution between a gaseous mobile phase and a solid or liquid stationary phase (EPA 1983). Following separation in the GC column, sample components are identified and quantified by a detection system such as flame ionization detection (FID), ultraviolet absorption spectroscopy (UV), or mass spectrometry (MS). These techniques are detailed in NIOSH (1984) and EPA (1983, 1984a).

HPLC is an analytical method in which components are separated based on their polarity (EPA 1983). Reverse-phase HPLC, which is used more widely for the analysis of PAHs, uses a nonpolar stationary phase and a polar mobile phase; hydrophilic components are eluted earlier than hydrophobic components. The detection systems most appropriate for HPLC analysis of PAHs are UV absorption spectroscopy and fluorescence spectroscopy (FS).

Thin-layer chromatography (TLC) has also been used to analyze for PAHs. With quasilinear luminescence methods (QLL), quasilinear spectra can be obtained for PAHs at liquid nitrogen temperatures (Sawicki 1976).

Table 8.1. Methods for analysis of dibenz[a,h]anthracene in environmental media

Media	Sample preparation	Analytical method[a]	Detection limit	Accuracy[b]	References
Air	Ultrasonic extraction with cyclohexane	HPLC	3 ng/m^3 (1500-m sample)	95%	NIOSH 1984 (Method 5506)
	Soxhlet extraction with benzene-methanol	GC/MS	0.05 ng/m^3	NA	Matsumoto and Kashimoto 1985
	Extraction with solvent	GC/MS	NA	NA	NIOSH 1984 (Method 5515)
	Soxhlet extraction with dichloromethane	TLC/FS	0.1 ng/g suspended particulate matter	NA	Katz 1979
Water	Extraction with methylene chloride	HPLC/FS	0.03 µg/L	~41%[c]	EPA 1984a (Method 610)
		UV	4 µg/L	76-135%	Riggin and Strup 1984
	Extraction with methylene chloride at pH <2 and pH >11	GC/MS	2.5 µg/L	~88%[c]	EPA 1984a (Method 625)
	Extraction with methylene chloride at pH 12-13	GC/MS	2 µg/L	NA	EPA 1984a (Method 1625)
	and pH <2	GC/MS	NA	NA	EPA 1986a
	Extraction with dichloro-methane	HPLC/UV	4 pg	NA	Ogan et al. 1979
	Extraction with cyclohexane	TLC/FS	0.5-1 ng/L	NA	Borneff and Kunte 1979
Soil	Extraction with *n*-pentane	TLC/UV	NA	NA	Butler et al. 1984
	Extraction with methylene chloride	GC/MS	NA	NA	EPA 1986a
Food	Extraction with isooctane	TLC/UV	0.2 µg/kg	NA	Howard 1979

[a]Abbreviations: HPLC, high-performance liquid chromatography; TLC, thin-layer chromatography; FS, fluorescence spectroscopy; GC, gas chromatography; MS, mass spectrometry; UV, ultraviolet absorption spectroscopy.
[b]NA = Not available.
[c]In large samples.

GC and HPLC are the chromatographic methods routinely used for the determination of 10 to 20 of the major PAHs in air and water samples. Detailed analysis of major and minor PAHs in a complex PAH mixture requires a combination of chromatographic techniques (Wise et al. 1986). GC/MS has a detection limit of greater than 10 pg; HPLC/FS has an approximate detection limit for PAHs of 25-50 pg (Santodonato et al. 1981). Das and Thomas (1978) reported a detection limit (twice the signal-to-noise ratio) of 2.3 pg using HPLC/FS for DB[a,h]A from a synthetic PAH mixture.

HPLC (5506) or GC/MS (5515) are the methods recommended by NIOSH (1984) for analyzing PAHs in workplace air. These methods incorporate a sampling train consisting of a filter and a solid sorbent (NIOSH 1984). The use of a high-volume sampler to sample a large quantity of air allows for detection of small amounts of PAH. The analytical methods required by EPA (1984a) for the analysis of DB[a,h]A in water are procedures 610 (HPLC/FS), 625 (GC/MS), and 1625 (GC/MS). These are required test procedures for municipal and industrial wastewater-discharging sites under the Clean Water Act. GC/MS is also the method required by the EPA Contract Laboratory Program for analysis of DB[a,h]A and other PAHs in water and soil. The Contract Required Quantitation Limit (CRQL) for DB[a,h]A in water is 10 μg/L; in soil/sediment, it is 330 μg/kg (EPA 1986a).

8.2 BIOLOGICAL SAMPLES

The available biological monitoring techniques are useful for detecting whether occupational or environmental exposure to PAHs has occurred, but because there have been no population-based studies to determine normal levels of PAHs, it is not yet possible to predict environmental exposure from body PAH levels or to predict what health effects are likely to be associated with these levels. In general, techniques that measure PAH or PAH metabolite concentrations in the urine are most appropriate for use in determining occupational exposure, since a high level of PAH exposure is necessary to result in the presence of these compounds in the urine. Methods that detect diol epoxide-DNA adducts are more sensitive to low exposure levels and are most appropriate for use in determining environmental exposure. The techniques presently available for determining exposure to PAHs are summarized in Table 8.2 and discussed in detail below.

Modica et al. (1982) and Bartosek et al. (1984) examined PAHs present in blood, mammary, adipose, liver, and brain tissue from orally exposed rats using gas-liquid chromatography with a flame-ionization detector. Examples of determination of PAH concentrations in human tissue samples using this technique were not located in the available literature. The detection limit for this method was not reported.

In mammalian systems, DB[a,h]A is converted by specific cellular enzymes to *trans*-dihydrodiols. These dihydrodiols are further converted to diol epoxides that are capable of binding to DNA (MacNicoll et al. 1979). HPLC can be used to determine radiolabeled DB[a,h]A diol epoxide adducts to DNA in vitro and in vivo (Liptay-Reuter et al. 1985). DB[a,h]A-DNA adducts have been found in lung and spleen tissue from

Table 8.2. Methods for analysis of PAHs in biological samples

Medium	Technique	Measured parameter	References
Tissue	Gas chromatography	PAH concentration	Modica et al. 1982, Bartosek et al. 1984
	Postlabeling of DNA	PAH diol epoxide-DNA adducts	Randerath et al. 1985, Randerath et al. 1986
	High-performance liquid chromatography	PAH diol epoxide-DNA adducts	Liptay-Reuter et al. 1985
Blood	Immunoassay	Antibodies to diol epoxide-DNA adducts	Harris 1985a,b, Harris et al. 1985, Harris et al. 1986
Urine	Gas chromatography	PAH concentration	Clonfero et al. 1986
	High-performance liquid chromatography	PAH concentration	Becher and Bjorseth 1983, Becher et al. 1984

mice fed DB[a,h]A for 2 weeks (Liptay-Reuter et al. 1985). Phillips et al. (1979) found that in mouse skin, DB[a,h]A bound to DNA to the extent of 15 pmol/mg DNA. Harris (1985a) reported that DB[a,h]A can be activated to form DNA adducts in cultured human tissues, including the bronchus, colon, and esophagus.

Randerath et al. (1985, 1986) examined PAH-DNA adducts in skin tissue from mice dermally treated with cigarette smoke condensate, and in placenta, bronchus, and larynx tissue from smokers using the DNA postlabeling technique. In this technique, radioactivity (^{32}P) is incorporated into the DNA removed from the exposed cells, and the digested DNA is separated using thin-layer chromatography. Quantitation of the adducts is achieved by scintillation counting. Small amounts of DNA are needed for analysis. These techniques have not been examined in humans or in actual biological samples to determine if abnormal levels can be detected.

Procedures are currently available that examine the presence of antibodies to DNA adducts in the blood using enzymatic immunoassays (Harris 1985a,b; Harris et al. 1985, 1986). Harris (1985b) developed a technique for determining human exposure to PAHs by detecting antibodies in sera to diol epoxide-DNA adducts using an immunoassay. The technique was tested on coke oven workers exposed to substantial amounts of benzo[a]pyrene and other PAHs in the work atmosphere, both in smokers and nonsmokers. Antibodies to benzo[a]pyrene diol epoxide-DNA adducts were quantified by enzyme-linked immunosorbent assay (ELISA). Higher proportions of sera positive for antibodies were found in a group of smokers and in the occupationally exposed group.

The urine of exposed humans was examined for the presence of PAHs. Polycyclic aromatic hydrocarbons and their metabolites can be extracted from urine and analyzed using HPLC/FS or GC/MS. DB[a,h]A was found in the urine of workers exposed to PAHs in an aluminum plant. However, environmental exposure could not be determined from urine DB[a,h]A content because high environmental concentrations of PAHs in the workplace were not found to be reflected to the same extent in excretion of PAHs in the urine (Becher and Bjorseth 1983, Becher et al. 1984). This problem was suggested to result from the nonbioavailability of particle-bound DB[a,h]A; therefore, this method may still be applicable in other exposure situations. PAHs have also been detected in the urine of individuals therapeutically treated with crude coal tar (Clonfero et al. 1986). However, this is not necessarily a useful test for occupational exposure because high levels of PAHs in the coal tar were necessary to concentrate PAHs in the urine.

Vo-Dinh et al. (1987) developed an antibody-based fiber-optics biosensor that can be used to detect benzo[a]pyrene or other PAHs in sample solutions. In this technique, antibodies to benzo[a]pyrene were covalently bound to the tip of the sensing probe. A helium-cadmium laser excites the molecules of benzo[a]pyrene bound to the antibodies, and the resulting fluorescence of these molecules is recorded by a photomultiplier; the intensity of the fluorescence signal is proportional to the amount of antigen bound to the sensor tip. The fiber-optics device can detect 1 femtomole (fmol; one-quadrillionth of a mole) benzo[a]pyrene in a 5-μL sample drop. This technique can be useful

in the assessment of an individual's exposure to benzo[a]pyrene and other PAHs, provided appropriate antibodies are used.

9. REGULATORY AND ADVISORY STATUS

Regulatory standards have been developed for the carcinogenic PAHs in the benzene or cyclohexane soluble fraction of coal tar pitch volatiles containing anthracene, benzo[a]pyrene, phenanthrene, acridine, chrysene, and pyrene. Therefore, these standards are not specific for DB[a,h]A. However, the regulatory standards were developed to regulate exposures to all PAHs in coal tar pitch volatiles and are appropriate for DB[a,h]A. These standards and advisory levels are presented in Table 9.1.

Dibenz[a,h]anthracene has been shown to be carcinogenic in experimental animals and undergoes metabolism to reactive electrophiles capable of binding covalently to DNA and inducing bacterial mutation and DNA damage. IARC (1973) classified DB[a,h]A in Group 2B because of sufficient evidence of carcinogenicity in experimental animals. IARC (1985) has concluded that there is sufficient evidence in experimental animals of the carcinogenicity of coal tars, creosote, and coal tar pitches. IARC also determined that there is sufficient evidence that occupational exposure to coal tars and coal tar pitch is associated with skin cancer; there is limited evidence of the carcinogenicity of creosote in occupationally exposed individuals (IARC 1985).

9.1 INTERNATIONAL

The World Health Organization (WHO) European standards for drinking water recommend a concentration of PAHs not to exceed 0.2 μg/L. This is based on the composite of six PAHs in drinking water: fluoranthene, benzo[a]pyrene, benzo[g,h,i]perylene, benzo[b]fluoranthene, benzo[k]fluoranthene, and indeno[1,2,3-cd]pyrene (WHO 1971). This limit was not chosen on the basis of potential health effects.

9.2 NATIONAL

9.2.1 Regulatory Standards

Coal tar, coal tar pitch, and creosote are considered by NIOSH and EPA to be human carcinogens (NIOSH 1977; EPA 1978, 1981, 1984c, 1986b). NIOSH reviewed epidemiologic and experimental toxicological evidence and concluded that inhalation exposure to these coal products, which contain a number of PAHs, increases the risk of lung and skin cancer in workers (NIOSH 1977). The Secretary of Labor has taken the position that no safe occupational exposure can be established for a carcinogen.

The current workroom air standard determined by the Occupational Safety and Health Administration (OSHA) is an 8-h, time-weighted average permissible exposure limit (PEL) of 0.2 mg/m^3 for the benzene-soluble

Table 9.1. Regulatory standards and advisory levels

Regulatory standard or advisory level	Basis	Concentration or risk coefficient	References
	Air		
Regulatory standard:			
8-h, Time-weighted average permissible exposure limit (PEL)	Benzene soluble fraction of coal tar pitch volatiles	0.2 mg/m^3	29 CFR 1910.1002 (OSHA 1985)
Advisory levels:			
8-h, Time-weighted average threshold limit value	Benzene soluble fraction of coal tar pitch volatiles	0.2 mg/m^3	ACGIH 1986
10-h, Time-weighted average threshold limit value	Cyclohexane soluble fraction of coal tar pitch volatiles	0.1 mg/m^3	NIOSH 1977
	Water		
Advisory levels:			
Ambient water quality criterion	Total carcinogenic PAHs	0 (28, 2.8, and 0.28 ng/L)[a]	EPA 1980

[a]The EPA recommended concentration for ambient water is zero. However, because attainment of this level may not be possible to achieve, the EPA estimated concentrations of total carcinogenic PAHs for ambient water corresponding to a 10^{-5}, 10^{-6}, and 10^{-7} upper-bound lifetime excess risk estimate, respectively, are presented.

fraction of coal tar pitch volatiles (29 CFR 1910.1002) (OSHA 1985). The PEL was established to minimize exposure to those PAHs believed to be carcinogens.

9.2.2 Advisory Levels

9.2.2.1 Air advisory levels

ACGIH time-weighted average threshold limit value. The American Conference of Governmental Industrial Hygienists (ACGIH 1986) recommended a time-weighted average threshold limit value (TLV) for occupational exposure to coal tar pitch volatiles based on an 8-h workday and 40-h week. The ACGIH time-weighted average TLV of 0.2 mg/m^3 is based on the benzene soluble fraction of coal tar pitch volatiles (including benzo[a]pyrene, anthracene, phenanthrene, acridine, chrysene, and pyrene). The TLV is based upon the ACGIH conclusion that at concentrations below 0.2 mg/m^3, any increase in the incidence of lung tumors and other tumors caused by occupational exposure to coal tar pitch volatiles should be minimal.

NIOSH time-weighted average threshold limit value. The National Institute for Occupational Safety and Health examined the epidemiologic and experimental toxicological evidence on coal tar, coal tar pitch, and creosote and concluded that they are carcinogenic to experimental animals and, potentially, to humans (NIOSH 1977). Polynuclear hydrocarbons have been identified in coal tar products. Because of the carcinogenic potential of these compounds, NIOSH recommended that the permissible exposure limit be set at the lowest concentration detected by the NIOSH recommended method of environmental monitoring, 0.1 mg/m^3 (NIOSH 1977). NIOSH proposed this time-weighted average threshold limit value to reduce the risk of cancer associated with exposure to coal tar products in the workplace.

9.2.2.2 Water advisory levels

Ambient water quality criterion. EPA (1980) developed ambient water quality criteria (AWQC) to protect human health from the potential carcinogenic effects caused by exposure to carcinogenic PAHs through ingestion of contaminated water and contaminated aquatic organisms.

DB[a,h]A is a known animal carcinogen. Because there is no recognized safe concentration for a human carcinogen, EPA (1980) recommended that the sum of the concentrations of total carcinogenic PAHs in water be zero. However, EPA (1980) recognized that a zero concentration level may not be possible to attain. The present criteria for total carcinogenic PAHs are based on the carcinogenicity assay reported by Neal and Rigdon (1967) in which stomach tumors developed in CFW-Swiss mice exposed to doses of 1-250 ppm benzo[a]pyrene in the diet, with a statistically higher incidence than controls. Assuming that an individual consumes 2 L of water and 6.5 g fish and shellfish each day, the sum of the concentrations of total carcinogenic PAHs corresponding to upper-bound lifetime excess cancer risks of 10^{-5}, 10^{-6}, and 10^{-7} are 28, 2.8, and 0.28 ng/L, respectively.

9.2.2.3 Food advisory levels

No food advisory levels for DB[a,h]A were located in the available literature.

9.2.2.4 Other guidance

Sections 103(a) and 103(b) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) require that persons in charge of vessels or facilities from which a hazardous substance has been released in quantities that are equal to or greater than its reportable quantity immediately notify the National Response Center of the release. Potential carcinogens are grouped into high-, medium-, or low-hazard categories on the basis of the biological information available. The reportable quantity for DB[a,h]A is 1 lb (EPA 1987).

9.2.3 Data Analysis

9.2.3.1 Carcinogenic potency

Although EPA previously published inhalation and oral cancer risk estimates for benzo[a]pyrene (EPA 1984b) based on the studies of Thyssen et al. (1981) and Neal and Rigdon (1967), these numbers are currently under review and have not been included here pending recalculation.

9.3 STATE

No state regulations or advisory guidance levels that apply to DB[a,h]A were located in the available literature. (Regulations and advisory guidance from the states were still being compiled at the time of printing.)

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11. GLOSSARY

Acute Exposure--Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Bioconcentration Factor (BCF)--The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same time period.

Carcinogen--A chemical capable of inducing cancer.

Ceiling value (CL)--A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure--Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity--The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

Frank Effect Level (FEL)--That level of exposure which produces a statistically or biologically significant increase in frequency or severity of unmistakable adverse effects, such as irreversible functional impairment or mortality, in an exposed population when compared with its appropriate control.

EPA Health Advisory--An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH)--The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure--Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

Immunologic Toxicity--The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro--Isolated from the living organism and artificially maintained, as in a test tube.

In vivo--Occurring within the living organism.

Key Study--An animal or human toxicological study that best illustrates the nature of the adverse effects produced and the doses associated with those effects.

Lethal Concentration(LO) (LC_{LO})--The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration(50) (LC_{50})--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose(LO) (LD_{LO})--The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose(50) (LD_{50})--The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lowest-Observed-Effect Level (LOEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of effects between the exposed population and its appropriate control.

Malformations--Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level--An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen--A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity--The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-Observed-Effect Level (NOEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of effects seen between the exposed population and its appropriate control.

Permissible Exposure Limit (PEL)--An allowable exposure level in workplace air averaged over an 8-h shift.

q_1^*--The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1^* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually $\mu g/L$ for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD)--An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)--The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-h period.

Reproductive Toxicity--The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL)--The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity--This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen--A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)--A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA)--An allowable exposure concentration averaged over a normal 8-h workday or 40-h workweek.

Uncertainty Factor (UF)--A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of humans, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX: PEER REVIEW

A peer review panel was assembled for dibenz[a,h]anthracene. The panel consisted of the following members: Dr. J. S. Felton, Lawrence Livermore National Laboratory; Dr. Dietrich Hoffmann, Naylor Dana Institute for Disease Prevention; and Dr. Alexander Wood, Roche Institute of Molecular Biology. These experts collectively have knowledge of DB[a,h]A's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.